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THE CAUSE AND TREATMENT OF HEMORRHAGE

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HEMORRHAGE forever has been a great problem, especially on the battle field. The ancient Greeks employed a vegetable styptic which, at the same time, was an anodyne that could be applied to the bleeding wound. Alum dissolved in vinegar, galls and the green bark of the fig tree were remedies recommended by Hippocrates. Celsus, the well known Roman surgeon, recommended cauterization by means of a red-hot instrument, and the surgeons of the fifteenth century still relied on the red-hot cautery; but the mortality from hemorrhage on the battlefield was as enormous as the treatment was horrible. It included the use of boiling oil, heated pitch and tar. Then a Swiss surgeon, Felix Wüertz, who strongly opposed the cruel use of the cautery as aggravating pain, recommended a new treatment, the use of a dressing composed of crocus martis (oxide of iron), alum and the white hair of a rabbit. It was not until the sixteenth century that Ambroise Paré, the father of French surgery, initiated a great advance; on the battlefields of Damvilliers in 1552 he used the ligature to arrest bleeding. This new procedure, like many other innovations, met with violent opposition.

Since the early seventeenth century when the celebrated English physician, Harvey, discovered the circulation of blood, many discoveries have been made regarding the cause of hemorrhage, the mechanism of blood coagulation, the arrest of hemorrhage and the treatment of hemorrhagic diseases.

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Etiology of Hemorrhage

By far the greatest cause of hemorrhage is trauma. Only in comparatively rare instances is hemorrhage due to vascular defects and an inadequacy in the process of the coagulation of the blood.

Trauma

Trauma, whether accidental or operative in nature, is accompanied by injury to blood vessels. The bleeding associated with injured blood vessels may stop spontaneously by the contraction mechanism of the vessel, the accumulation of platelets and agglutination at the point of injury. This temporarily plugs the open vessel and aids in the formation of a clot.

Fragility of Blood Vessels

Capillary resistance is lowered in a number of diseases such as scarlet fever, measles, in some cases of chronic renal and liver diseases and especially in scurvy. In scurvy the fragility of the blood vessels, according to Rapaport[1] and Vacek,[2] is believed not to be due to ascorbic acid deficiency, as generally supposed, but to the lack of a second factor, vitamin P or citrin. Capillary fragility also is increased before the commencement of the menstrual period, according to Wright and Lilienfeld,[3] a fact that should be kept in mind when planning the extraction of teeth during menstruation.

In addition to these conditions, in which there are generally no disturbances of coagulation, there are other diseases in which capillary fragility plays an important part, but in which the principal cause of the disease is a defect in the coagulation mechanism. This is true of many types of purpura and leukemia. In both there is an increased permeability of the vessels which allows the extravasation of blood and accounts for the hemorrhages and ecchymoses so often seen in the mucous membranes of the mouths of these patients.

Defects in the Coagulation Mechanism of Blood

A defective coagulation mechanism is seen in many well known but rather rare clinical diseases. The following is a classification of hemorrhagic diseases attributed to defects in the coagulation mechanism of the blood, according to Quick.[4]

I. Diminished prothrombin (prothrombinopenia)
   A. Lack of vitamin P
      1. Dietary origin—absence of bacteria in intestines
         a. Hemorrhagic disease of the newborn
      2. Faulty absorption—lack of bile salts
         a. Obstructive jaundice
         b. Biliary fistula
         c. Sprue

1. Rapaport, H. G., Vitamin P and Capillary Fragility. *J. Pediat.* 18:321 (March) 1941.
2. Vacek, V., New Data on Vitamin P. *Schweiz. med. Wchnschr.* 71:155 (February) 1941.
3. Wright, S., and Lilienfeld, A., Pharmacologic and Therapeutic Properties of Crystalline Vitamin C. *Arch. Int. Med.* 57:241 (February) 1936.
4. Quick, A. J., A Classification of Hemorrhagic Diseases Due to Defects in the Coagulation Mechanism of the Blood. *Am. J. M. Sci.* 199:118 (January) 1940.

B. Liver damage—faulty utilization of vitamin K
   1. Postanesthetic liver damage
   2. Chloroform poisoning
   3. Acute yellow atrophy

II. Changes in concentration of calcium in blood
   A. Hemophilia calcipriva (a theoretic disorder)

III. Deficiency of thromboplastin (thromboplastinopenia)
   A. Diminished number of platelets
      1. Thrombocytopenia (various forms of thrombocytopenic purpura)
   B. Increased resistance of platelets causing lack of thromboplastin and coagulation
      1. Hemophilia

IV. Decreased fibrinogen (fibrinogenopenia)
   A. Acquired fibrinogenopenia
      1. Nutritional deficiencies
      2. Diseases of the blood-forming organ
      3. Severe liver damage
      4. Snake bite
   B. Congenital fibrinogenopenia

V. Anticoagulants in the blood
   A. Liberation of heparin into the blood
   B. Administration of heparin or dicoumarin

Theories of Coagulation of the Blood

In order to understand the cause and treatment of hemorrhage and hemorrhagic diseases, it is necessary first to have a clear picture of the physical and chemical changes that occur in the formation of a blood clot. Coagulation, according to Eagle,[5] involves two reactions: (1) the formation of an active coagulant, thrombin; and (2) the formation of fibrin by an interaction between thrombin and fibrinogen.

Thrombin.—The formation of thrombin depends on the interaction of at least three factors: (1) thromboplastin, a substance derived from the platelets but which is also present in tissue; (2) calcium ions, and (3) prothrombin, a plasma factor which is formed in the liver.

1. Thromboplastin is a lipoprotein which is found in many tissues of the body as an intracellular substance. Besides in the platelets, it also is found in the brain, lungs, thymus and muscles. It does not occur in a free state but is liberated when tissue cells are injured.

2. Calcium ions are considered necessary in the clotting of blood; however, thrombin can be prepared which contains no analytically demonstrable calcium. *In vitro* the addition to blood of sodium citrate prevents clotting because it combines with calcium ions and inactivates the latter.

3. Prothrombin is formed particularly in the liver and to some extent in the bone marrow. It is regarded as a protein and is found in many times the concentration required to coagulate blood. It is a thermolabile substance, the formation of which is governed in some way by the antihemorrhagic vitamin K. Vitamin K is derived from two sources, namely: the diet, especially green leaves, cauliflower and cabbage, and by synthesis in the intestinal tract by the action

5. Eagle, H., Recent Advances in the Blood Coagulation Problem. *Medicine* 16:95 (May) 1937.

UMI

of bacteria on the intestinal contents. Vitamin K, if ingested, depends on the presence of bile salts for its absorption and use. Failure of its absorption results in a reduction in the amount of prothrombin in the blood which leads to a prolonged coagulation time. One remedy is the administration of both vitamin K and bile salts.

Fibrinogen.—This is a labile plasma protein formed in the liver and found in the plasma of circulating blood. It can be observed if blood is put on a slide. A gel-like structure forms, a coagulum of fibrin which with the remainder of the blood forms an elastic structure, the blood clot. In disease of the liver fibrinogen will be decreased to such an extent that excessive bleeding results.

Platelets.—The blood platelets should be mentioned separately since they play a very important role in hemostasis, particularly in all known functions to control loss of blood. Through the process of agglutination the platelets seal the injured vessel; through the liberation of thromboplastin they initiate coagulation. Because they must be traumatized to liberate thromboplastin, clotting is prevented if their resistance is high, as it is in hemophilia. The platelets are derived from megakaryocytes of the bone marrow. The normal platelet count is about 250,000 per cubic millimeter of blood. They are believed to be destroyed by the spleen; for this reason splenectomy is recommended in some cases of thrombocytopenic purpura in which platelets are very low or absent. After a splenectomy is performed, a regeneration rate as high as 1,000,000 per cubic millimeter in twenty-four hours has been reported.

Anticoagulants.—Heparin is the anticoagulant found in the body, especially in the liver and in relatively large amounts in the lungs, muscles and intestinal wall, and is present in small amounts in the blood. It should be remembered that anticoagulants such as heparin and dicoumarin frequently are given as preventives of thrombophlebitis, to decrease the coagulability of the blood, and that an emergency tooth extraction in a patient so treated may be complicated by hemorrhage difficult to control.

Diagnosis of Disturbances of Coagulation

The following are the most common methods used to study the various factors concerned in hemorrhagic disorders:

Coagulation Time.—By this test the clotting of the blood is measured. The blood is obtained either by skin puncture or, if great accuracy is required, by venipuncture. The capillary tube method generally is used. A simple test consists of putting two drops of blood on a glass slide and passing a needle through it every minute. When a piece of fibrin thus is removed, coagulation has started. The normal is two to four minutes. For accurate determination the method of Pohle and Taylor[6] is recommended, since it avoids the admixture with tissue juices which hasten clotting. The normal quotient by this method is six to twelve minutes.

Bleeding Time.—A drop of blood is absorbed from a cut, such as in the lobe of the ear, every half minute until the drops cease to form. The normal is two to eight minutes.

Prothrombin Time.—Coagulation time does not differentiate between the various factors that disturb the clotting mechanism. The deficiency in prothrombin

6. Pohle, F. J., and Taylor, F. H. L., Coagulation Defect in Hemophilia. Effect in Hemophilia of Intramuscular Administration of Globulin Substance Derived from Normal Human Plasma. *J. Clin. Investigation* 16:741 (September) 1937.

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should be recognized. Quick[4] devised the following test which is in common use today.

Place 0.5 cc. sodium oxylate solution (1.34 Gm. of anhydrous sodium oxylate in 100 cc. of distilled water) in a tube marked to hold exactly 5 cc. Blood which is withdrawn by venipuncture is added in the amount of 4.5 cc., and the two are mixed thoroughly by inverting two or three times. After it is centrifuged a few minutes, 0.1 cc. of the clear plasma which has separated is transferred to a serologic tube, and to it is added 0.1 cc. of thromboplastin extract (prepared from rabbit brain). Then it is heated to 37.5 C. Add quickly 0.1 cc. of calcium chloride solution (1.11 Gm. of anhydrous calcium chloride in 400 cc. of distilled water) and accurately measure with a stopwatch the number of seconds that elapse between the time the calcium is added and the formation of the clot. The normal is sixteen to seventeen seconds.

Clot Retraction Time.—Three cc. of blood are put into a test tube and placed in an incubator at 37 C. The tube is inspected hourly and the time at which retraction occurs is noted. If the blood is normal the clotting process should be completed after eighteen to twenty-four hours. The retraction is due to the presence of blood platelets and is independent of the coagulation time. In thrombocytopenia the coagulation time may be normal, but the blood clot will be friable and retract very little or not at all, even after several days. In hemophilia the blood coagulates very slowly, but the clot when once formed has normal retractile power.

Blood Cell Counts.—Microscopic examination of blood and stained blood is of value in order to diagnose blood diseases, especially the anemias, leukemias

Fig. 1.—Tourniquet test used on patient with purpura hemorrhagica. Note hemorrhagic petechiae on forearm

and purpuras. In the anemias the erthyrocyte count is reduced to 2,000,000 or lower, and the cells may be irregular in size, shape and color. In leukemia the affected cells in circulation are increased markedly in number, up to several hundred thousand, and there may be many immature forms. In purpura hemorrhagica a decrease in the platelet count is the characteristic feature.

Interpretation of Findings

Prolonged Coagulation Time.—This occurs in hemophilia, where it is from one to several hours, in the anemias, leukemias, in many infectious diseases and in jaundice. Prolonged coagulation time slightly above the normal may occur in healthy individuals and may be the cause of prolonged oozing from small blood vessels, as in cases of tonsillectomy, operative procedures in the mouth or the extraction of teeth.

Prolonged Bleeding Time.—Bleeding time does not always parallel clotting time. There is a slight increase in the severe anemias. A great increase, ten to ninety minutes, is found in patients with blood platelets greatly reduced (purpura hemorrhagica, acute leukemia) and in patients with the fibrinogen content of the blood extremely low (phosphorus poisoning, destructive liver disease).

The paradox of prolonged bleeding time and normal coagulation time is explained by the fact that, in a disease such as thrombocytopenic purpura, the number of platelets is too small to plug the defect in the capillaries but large enough to initiate the process of coagulation.

Prothrombin Determination.—This factor is of value to determine the state of prothrombinopenia which may arise from lack of vitamin K, because of dietary deficiency or faulty absorption caused by the lack of bile salts such as occurs in obstructive jaundice, biliary fistula and sprue or in cases in which liver damage has been produced. Here should be mentioned the effect of the prolonged use of acetylsalicylic acid (aspirin) which may decrease the prothrombin. Prothrombinopenia may be corrected in such cases by the administration of vitamin K. Cahn[7] recommended that 1 mg. of vitamin K should be prescribed to every 5 gr. of aspirin, if taken repeatedly.

The Tourniquet Test.—This test, when abnormal, shows an excessive capillary fragility which may be caused by a vascular defect (scurvy) or a lack of platelets needed to maintain capillary integrity under increased pressure, as seen in purpura hemorrhagica (Fig. 1).

Diseases Which Predispose to Hemorrhage

The history of the patient and family history may disclose hemorrhagic tendencies. Patients should be questioned carefully as to their reactions to injuries. Have they bled severely from minor cuts? Have they been bruised easily? Has any member of the family had unusual bleeding after tooth extraction and, if so, have they had similar experiences of bleeding from wounds in other parts of the body? If the patient has arteriosclerosis, the capillaries lose their contractility; in patients with hypertension bleeding is likely to be more severe than in those with normal blood pressure.

Trauma.—In accidental trauma contusions, lacerations, fractures and other injuries may cause hemorrhage from the skin, oral mucous membranes or bone (Fig. 2). In addition, all oral surgical operative procedures represent traumatic

7. Cahn, L. S., Acetylsalicylic Acid (Aspirin) as a Cause of Bleeding. *J. Oral Surg.* 3:336 (October) 1945.

Fig. 2.—Patient injured in automobile collision showing hemorrhage from nose and lacerations of the face

injuries. The extraction of teeth plays an important part, particularly if associated with excessive trauma of the alveolar bone or the gingiva. The bleeding is exaggerated by local inflammation such as gingivitis, periodontitis, stomatitis, alveolar abscess, malignant growths and by hemorrhagic diseases of a general nature.

Scurvy.—This disease, caused by a deficiency of vitamin C or P, is characterized by great debility, loss of weight and regions of ecchymoses on the arms, legs, and trunk, which are of petechial nature but may become larger. The slightest bruise or injury causes bleeding, and periarticular hemorrhages may cause tender painful joints. There even may be subperiosteal hemorrhages along the shafts of the bones followed by necrosis.

The oral symptoms are significant and of diagnostic value. First, there is an inflammation of the gingivae with bleeding from the slightest irritation. The gingivae have a bluish purple appearance with regions of ecchymosis especially on the palate. Hematomas may form and the bloated gingivae may cover the teeth which become loose and finally denuded as the surrounding soft tissues become ulcerated.

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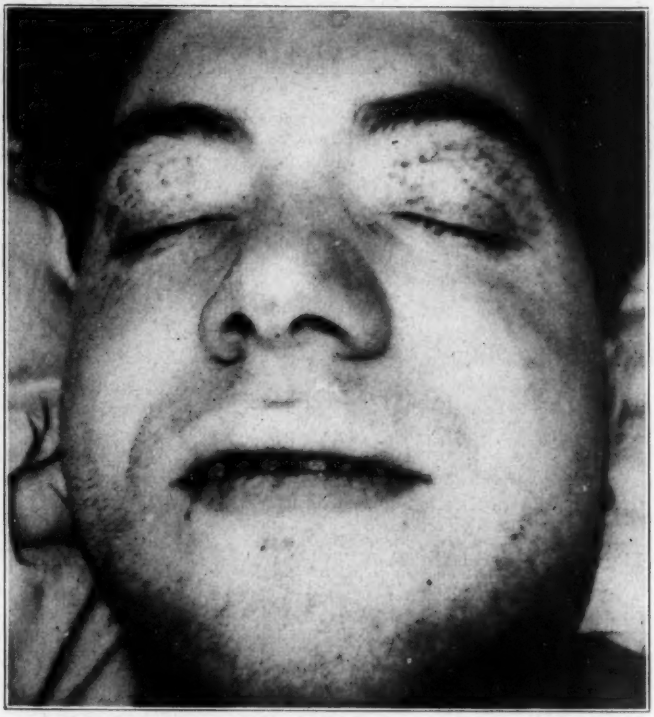

Fig. 4, Case 2.—Patient with thrombocytopenic purpura showing pin-point petechiae on the eyelids

Acute and chronic forms of myelogenous, lymphatic and monocytic leukemia are distinguished, and a fourth in which there is no leukocytosis, termed "aleukemic," is recognized.

In acute leukemia, purpuric manifestations involving the oral mucosa are found. Bleeding following slight trauma, petechiae and regions of ecchymosis are common; enlargement of the gingival papillae due to leukemic infiltration of the tissue and extensive necrosis which may develop into noma are seen. The oral tissues are subject to invasion by Vincent's organisms. Diffuse cellulitis may result. The skin generally shows petechial regions of ecchymosis and pustular and bullous lesions.

In the chronic forms of leukemia, thrombocytopenia may be present. Bleeding, however, occurs only in the late stages. Lymph nodes may be enlarged and tender, and there may be specific infiltration of the gingivae by leukemic cells. Ulcerations are likely to occur in the mouth, and tooth extraction is followed by prolonged hemorrhage and frequently by infection.

In leukemia, especially the acute form, the bleeding time is prolonged, clot retraction is poor and the tourniquet test is positive as in purpura. Differential diagnosis is made by the abnormality in examination of the white cells, which

Fig. 5, Case 3.—Patient with purpura hemorrhagica and chronic lymphatic leukemia. Note petechial spots on the face

shows both a marked increase, up to several hundred thousand cells per cubic millimeter, and abnormal and immature cells in circulation.

Agranulocytopenia or agranulocytosis often is associated with ulceration in the mouth and throat, and this has given rise to the name agranulocytic angina. A number of deaths have been recorded following tooth extraction. Patients often suffer spontaneous hemorrhages (as patient shown in Fig. 7).

Case 3—Purpura Hemorrhagica Associated with Chronic Lymphatic Leukemia

A 16 year old boy had acute gastroenteritis with lymphadenopathy of an undetermined cause in 1939. As a child he was thought to have Banti's disease for which a splenectomy was performed.

He came to the clinic exhibiting many petechial spots on his lips, palate (Fig. 6) and other parts of the body (Figs. 5 and 6). The white cell count was 25,000 with 70 per cent lymphoblasts. There were practically no platelets found on the smear. He also had enlarged lymph nodes in the neck and submaxillary regions, which were thought to be caused by lymphatic leukemia. The absence of blood platelets was believed to be caused by invasion of the bone marrow by lymphatic tissue.

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Anemia.—In pernicious anemia the red cell count may be lower than 2,000,000 and the platelet count lower than 100,000 per cubic millimeter. In these cases the bleeding time and prothrombin time are usually normal. Signs of purpura and prolonged bleeding after tooth extraction have been experienced. Harang[8] reports that of 15 patients with blood dyscrasias who entered the emergency room because of postoperative bleeding, 5 (33 per cent) were patients with pernicious anemia.

Aplastic anemia, which in some cases follows exposure to certain chemical and physical agents (benzol, arsenicals, gold compounds and other substances), has an insidious onset and predisposes to hemorrhage and infection. This depends on the degree of thrombocytopenia and granulocytopenia which may be associated with the disease. The erythrocyte count may be between 2,000,000 per cubic millimeter or lower, and the leukocyte count may be decreased greatly. When well advanced, bleeding from the nose, mouth and gastro-intestinal tract develops, hematomas may form and other signs of purpura may appear.

Hemophilia.—This is a sex-linked hereditary disease confined to males but transmitted through females, although there are sporadic cases known in females.

Other hemorrhagic familial disorders must be distinguished, such as hereditary thrombocytopenic purpura, multiple hereditary telangiectasis and nonhemophilic hereditary hemorrhagic diathesis.

In hemophiliacs the platelets are more resistant than normal, and therefore

8. Harang, H. L., Blood Dyscrasias in Relation to Secondary and Primary Hemorrhages, Postoperative. *Am. J. Orthodont. & Oral Surg.* (Oral Surg. Sect.) 30:775 (December) 1944.

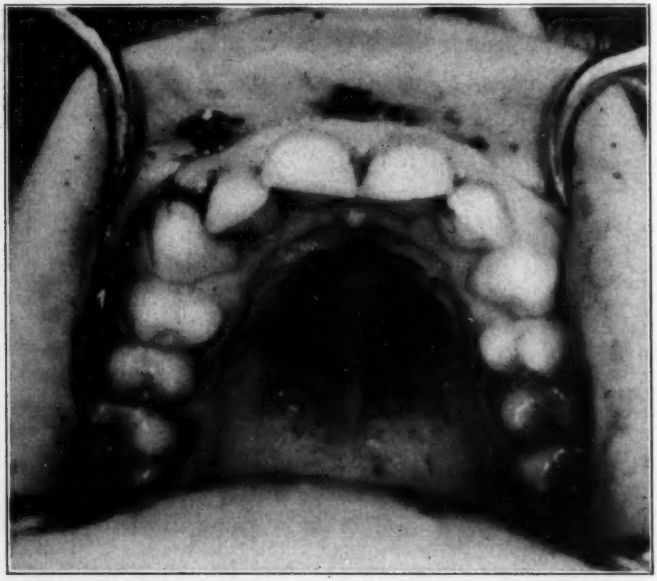

Fig. 6, Case 3.—Patient with purpuric hemorrhagica and chronic lymphatic leukemia. Note ecchymosis of palate

Fig. 7.—Patient with agranulocytosis causing spontaneous gingival hemorrhages

the thromboplastic substance is furnished less readily. Bendien[9] has found a substance precipitated by acid from normal plasma which he described as a coagulation globulin. Howell,[10] who freed it from protein, named it plasma thromboplastin. Very little of this substance is found in hemophiliacs. The coagulation time is delayed greatly (one to twelve hours). All other tests are generally normal including the bleeding time, since the thromboplastic derived from tissue juice is sufficient to produce coagulation of the small wound made for obtaining the blood for the test. In larger wounds and injuries of the mucosa, this factor is much less and hence the prolonged bleeding episodes. Spontaneous bleeding may occur (Fig. 8); the eruption of the teeth may be associated with hemorrhages lasting for days or weeks, and tooth extraction often is associated with bleeding to the extent of exsanguination.

Case 4—Tooth Extraction in a Hemophiliac

A 42 year old man came to the dental clinic on March 27, 1945, complaining of bleeding from the mouth. One week previously there had been spontaneous bleeding from around the teeth in the upper jaw. He was an alleged hemophiliac and was given vitamin K by his local physician without results. The patient reported having bled spontaneously at various times, with profuse bleeding from cuts. He had several brothers who also "bled easily." The patient had one son who was not a bleeder.

Examination.—A large blood clot the size of an egg yolk was observed on the lingual aspect of the anterior portion of the palate. The teeth were very carious and there were numerous roots present; all were covered with blood (Fig. 8). Hematologic examination showed a bleeding time of one minute, forty-five seconds; coagulation time, fifteen to twenty minutes; red cell count 3,400,000; white cell count 6,400.

9. Bendien, W. M., and van Creveld, D., On Some Factors of Blood Coagulation. *Acta med. Scandinav.* 99:12, 1939.
10. Howell, W. H., Theories of Blood Coagulation. *Physiol. Rev.* 15:435 (July) 1935.

Treatment.—The patient was admitted to the emergency ward where he was given a transfusion of fresh whole blood. On March 29 the patient was transferred to the house. Blood still was oozing from the gingivae but it had decreased in amount. On March 30 the blood examination showed: hemoglobin 70 per cent; red cell count 3,800,000; white cell count, 5,600; polymorphonuclear leukocytes 46 per cent; large and small lymphocytes 34 per cent; monocytes 12 per cent, eosinophils 8 per cent; platelets normal; coagulation time (2-tube) seven and a half minutes. He was given another transfusion of 500 cc. of fresh whole blood and the same amount again the next day.

On April 7, with the patient under gas, oxygen and ether anesthesia, the upper first premolar and first incisor were extracted. Bleeding was controlled locally with thrombin tyrothricin tablets placed in the sockets. Gauze packs were inserted between the dental archs to keep the tablets in position. The patient was given an intravenous infusion of 1,500 cc. of 5 per cent dextrose in water during the operation.

Course.—There was little bleeding after the operation. Two days later the hemoglobin count was 80 per cent. He was given another transfusion of 500 cc. of fresh whole blood, and six teeth were extracted with the aid of gas, oxygen and ether anesthesia. Thrombin tyrothricin tablets were used again for hemostasis. After the extraction he bled continuously and was given 500 cc. of whole blood. On the next day he was bleeding from the gingivae around other infected tooth roots but not from the extraction wounds.

He was given four more blood transfusions, and on two occasions he had a transfusion reaction with chills. He was discharged on April 19.

The patient was readmitted on April 27, again with bleeding from the gingivae around the teeth still present, but not from the recent extractions. There was a large clot forming around a decayed tooth on the alveolar ridge of the mandible (Fig. 9). The red cell count was 3,200,000; the white cell count 6,500, and the hemoglobin 60 per cent. He was given a transfusion of 150

Fig. 8, Case 4.—Patient with hemophilia and spontaneous hemorrhages from the gingivae

cc. of whole blood but again suffered from a reaction. On May 1 one tooth was extracted, and a week later two teeth were removed, with the patient under gas, oxygen, and ether anesthesia. He was given a transfusion of 500 cc. of whole blood before each extraction and one during the following week. He was discharged on May 15, when bleeding from the gingivae had stopped completely.

Patients Treated by Anticoagulants.—Occasionally a patient who is given heparin or dicoumarin because of arterial or venous thrombosis develops an alveolar or periodontal abscess. Extraction, of course, would be followed by prolonged bleeding and should not be undertaken except in an emergency. The anticoagulants should be omitted and local remedies applied.

Case 5—Abscess from Use of Anticoagulant

A man was admitted to the hospital on October 27, 1947, with a diagnosis of popliteal embolism of the left leg. He had been confined to bed most of the previous week because of a severe cold for which he was taking penicillin. On the morning of entry he was up and about when suddenly his left foot and lower leg felt cold and numb, with subsequent pain in the left calf and pallor of the left foot and lower leg.

Treatment.—On admission he received 150 mg. of heparin in Pitkin's menstruum intramuscularly and 200 mg. of dicoumarin by mouth. Anticoagulant therapy was continued until November 2, 1947, and the patient was to be discharged the following day. On November 4, however, he suddenly developed pain and numbness with pallor of the right leg. A diagnosis of embolism of the right femoral artery was made, and an embolectomy was performed. Post-

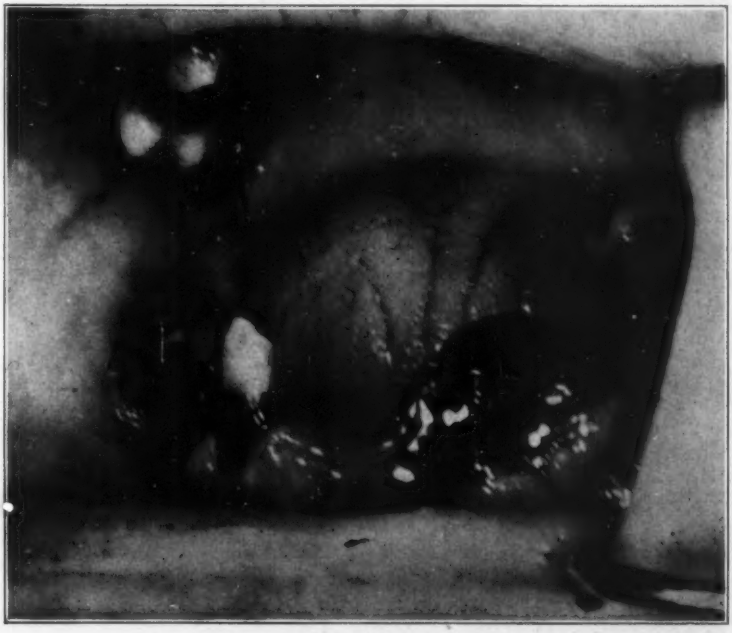

Fig. 9, Case 4.—Patient with hemophilia showing large clot forming around decayed teeth

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operative recovery was normal with no complications. The patient was discharged on November 12, 1947.

On December 11, 1947, the patient re-entered the hospital complaining of cold and numbness in the right foot, and a diagnosis of small arterial embolism of the right foot was made. He was given 20,000 units of heparin in 1,500 cc. of 5 per cent dextrose in water intravenously by the slow-drip method. After this 200 mg. of dicoumarin was administered on December 12 and 100 mg. daily thereafter. The clotting time during the administration of heparin went to eighty-six minutes by the five-tube method. The prothrombin time was elevated to twenty-three seconds.

Course.—On December 13, the patient developed a toothache in the left lower jaw. Since he was receiving anticoagulant therapy, it was decided to give only conservative treatment. He received codeine to control pain. Roentgenograms revealed a region of rarefaction around the root of the left mandibular first molar. On December 18, a swelling on the left side over the body of the mandible developed, with cellulitis. It was decided to extract the tooth. Dicoumarin was discontinued; this caused a drop in the prothrombin time to nineteen seconds with a clotting time within normal limits. The lower left first molar then was extracted, with the aid of Monocaine hydrochloride (Novocol) anesthesia, and thrombin and tyrothricin powder was inserted in the socket to aid coagulation.

Results.—There were no postoperative complications. The patient's condition improved; dicoumarin was discontinued permanently and he was discharged on December 24, 1947.

Nonhemophilic Hereditary Hemorrhage.—Hemorrhagic diathesis occurs in patients with perfectly normal hematologic findings except the bleeding time which is prolonged. They suffer from prolonged bleeding after injuries, especially the extraction of teeth. In some the tourniquet test is positive while the platelet count and coagulation times are normal. Offspring of either sex may be produced who inherit the disease. Levy[11] reported recently 4 cases with prolonged bleeding after extraction of teeth.

The Treatment of Oral Hemorrhage

The treatment of hemorrhage, whether spontaneous or caused by an operative procedure in the mouth, may be divided into:

1. Measures of a general nature used either for prophylactic reasons or to arrest a hemorrhage that occurred because of an accidental injury or operative procedure.
2. Local measures which often have to be used in conjunction with general therapy.

Systemic Treatment

The treatment should be directed first of all to the elimination of the cause of the hemorrhagic diathesis if present. Operations should be delayed if possible until a correction has been effected, but even then special precautions are indicated.

Patients with hemorrhagic diseases should be hospitalized. A thorough and complete blood study should be made. In cases of scurvy, ascorbic acid should be given, at least 500 mg. per day with vitamin P (citrin) to decrease the capillary fragility, and the diet should be adjusted.

In thrombocytopenic purpura splenectomy gives good immediate results and the platelet count increases almost immediately; however, not all cases are permanently cured. The diet should contain hemoglobin-building substances and

11. Levy, T. L., Nonhemophilic Hereditary Hemorrhagic Diathesis. *Ann. Int. Med.* 27:96 (July) 1947.

vitamins (liver, chicken gizzard, kidney, eggs, prunes and vegetables). Ascorbic acid and vitamin P may be of value to decrease the capillary fragility. If operative procedures are contemplated, fresh blood transfusions are valuable.

In secondary purpuras and hereditary hemorrhagic diathesis, splenectomy is of no value; transfusions are in order and the use of moccasin snake venom (Peck[12]) has been recommended.

In cases of pernicious anemia liver therapy is indicated (3 to 6 cc. per day intramuscularly for emergency treatment); in cases of hemorrhage associated with obstructive jaundice, vitamin K (4 mg. per day) with bile salts should be given.

In the leukemias blood transfusions to decrease the danger of hemorrhage in preparation for necessary tooth extraction are considered helpful.

In hemophilia a cure cannot be expected, but in anticipation of tooth extraction, or if the patient has started to bleed spontaneously, transfusions of fresh blood (twelve to twenty-four hours old) are recommended to reduce the coagulation time. Small amounts of blood (50 to 100 cc.) will reduce the coagulation time markedly. Such transfusions should be repeated frequently until the danger of hemorrhage has passed. They should be given preoperatively, during the operation and postoperatively.

Lewis and associates[13] reported from the Thorndike Memorial Laboratory that normal plasma contains a substance which is absent in hemophilic plasma and which is capable of shortening the coagulation time in the hemophiliac. It is believed to be a subfraction of the active globulin fraction with which it is associated. The globulin, or its fraction when available, may be applied locally to arrest bleeding.

In the plasma fractionation laboratory of the Department of Physical Chemistry, Harvard Medical School, an antihemophilic globulin, fraction I of normal blood plasma, has been developed for intravenous injection and is provided by the American Red Cross without charge. It will reduce the coagulation time to about fifteen to thirty minutes after the intravenous administration, according to direction, of two 5 cc. vials containing 200 mg. each of the substance which is diluted in 5 cc. of sterile water. If the improvement is not satisfactory, the injection is repeated after two hours. The extractions are performed as soon as the clotting time has been reduced properly and all the teeth that need to be extracted can be removed at once. The reduction of the clotting time persists for about four hours after which it slowly rises to its previously high level, or less in twenty-four hours. The injections may be repeated until the wound has healed completely. However, this treatment does not give uniformly good results, and it is believed by some hematologists that there is another factor lacking in hemophiliacs, such as a serum activator, which has not been discovered as yet but is being investigated currently.

Local Treatment

In hemorrhage caused by injury, hemostasis may be procured easily by clamping and tying the bleeding vessel or by electrocoagulation. Meticulous care should be taken to arrest all bleeding from soft tissue wounds, and often suturing is indicated. A sterile pack of gauze may be applied between the jaws. It is placed on the bleeding socket after tooth extraction or on an oozing wound which has

12. Peck, S. M., Rosenthal, N., and Erf, L. A., Purpura. *Arch. Dermat. & Syph.* 35:831 (May) 1937.
13. Lewis, J. H.; Davidson, C. S.; Minot, G. R.; Soulier, J. Q.; Tagnon, H. J., and Taylor, F. H., Chemical, Clinical, Immunological Studies on the Products of Human Plasma Fractionation. *J. Clin. Investigation* 25:870 (November) 1946.

been sutured, until the clot has formed. Bleeding from a tooth socket may be dealt with by placing thrombin or oxidized cellulose in the alveolus; the procedure will be described presently. Bleeding in bone operations may be arrested by condensing the bleeding spongiosa with a burnisher, or by placing bone wax in a bleeding region such as the mandibular canal. In serious bleeding from the anterior palatine artery, a peg may be inserted. Frequently the bleeding of the palatal mucosa can be arrested with a mattress suture taken through the mucosa around the bleeding vessel, tying it on the surface. In very serious hemorrhage, tying of the external carotid artery may have to be resorted to.

In case of secondary hemorrhage after tooth extraction, the socket should be debrided, all of the old clot removed and a pressure pack applied. The patient should be placed in a modified Fowler's position (approximately 9 or 10 inches' elevation) if in bed or should be directed to sit in a chair rather than lie down, to decrease the blood pressure in the head. Cold compresses applied to the region or to the neck are often useful. Rinsing the mouth should be prohibited. Careful approximation of the wound margins and the use of a splint are recommended, with the insertion of a hemostatic agent such as thrombin in the wound to prevent oozing of blood into the subcutaneous tissue causing disfiguring ecchymosis.

Various drugs have been recommended for local application. Epinephrine (1:1,000) generally is used for application during operation, and the injection of a local anesthetic with epinephrine before operation, even when general anesthesia is used, is recommended to secure hemostasis. The use of ferric subsulfate powder pressed into a socket with iodoform gauze and left for several days has, in the past, given good results, although the black precipitate is objectionable.

In patients with hemorrhagic diseases the bleeding may be arrested by the local application of fresh raw meat, fresh blood or cephalin. Beef or rabbit globulin can be applied on gauze to the socket and has been recommended as a great aid in such bleeding after tooth extraction. Today, fibrin foam or Gelfoam with thrombin may be used as an effective coagulant, especially if the wound can be closed over it by suture. Oxidized cellulose has been given a favorable report by Gwinn, Grimm and Ferber.[14] Since oxidized cellulose and Gelfoam used to apply the thrombin may be left in the wound permanently, the danger of new hemorrhage, which always is feared when a medicated gauze pack is removed, is eliminated.

Sharpe and Dohme's Thrombodent cones, containing the following active ingredients, thrombin (of human origin) 1 unit, and tyrothricin 1 mg., have been found extremely effective in my experience; the thrombin in one cone will clot 1 cc. of normal blood in less than one minute, and tyrothricin is an antibiotic agent effective against gram-positive and some gram-negative organisms that are found in the oral cavity. It destroys anaerobic and beta hemolytic streptococci which so frequently contaminate dental wounds. One to three are placed in a tooth socket, or if the bleeding occurs at the gingival margin they can be crushed to a powder and held in place by an intermaxillary pack. These local measures are of great help whether or not general medication and blood transfusions are used.

14. Gwinn, C. D., Grimm, D. H., and Ferber, E. W., Oral Use of Absorbable Oxidized Cellulose in the Treatment and Prevention of Postoperative Hemorrhage. *J.A.D.A.* 36:155 (February) 1948.

Conclusion

In conclusion it may be said that a modern understanding of hematology and a thorough diagnosis of the local and fundamental causes of bleeding will help a great deal to eliminate the danger of primary and secondary hemorrhages. The newly developed constituents of blood which are available today are great aids to the dental and oral surgeon. Both the antihemophilic globulin developed by the Department of Physical Chemistry, Harvard Medical School, and provided by the American Red Cross for intravenous use, and the local preparation, the fibrin and Gelfoam used to apply thrombin, as well as other coagulants, rabbit globulin (Lederle Company) and beef thrombin in powder form or combined with tyrothricin compressed into convenient cones (Sharp and Dohme), make up a useful armamentarium for the treatment of hemorrhage.—*1180 Beacon Street, Brookline.*

A METHOD FOR IRRIGATING THE MAXILLARY SINUS

A few years ago the author devised a simple but effective method for the irrigation and treatment of the maxillary sinus after it has been opened for operative procedure and then closed by returning the flap to its original position.

As an example, let it be assumed that a root tip is to be removed from an infected right antrum. A flap of desired size and position is laid back and a window cut in the underlying bone. The root is removed and any other necessary operative steps taken. The flap is returned to position and sutured. No counter opening has been made in the naso-antral wall.

Because the right sinus has been operated on, the patient is instructed to sleep on the left side, thus providing for drainage into the nasal fossa.

At the patient's next appointment, a 5 cc. Luer syringe is filled with the solution of choice. The patient is seated in an upright position and instructed to lean forward, at the same time tilting his head to the left. A point on the flap opposite the underlying window is selected, the needle inserted in the sinus and the contents of the syringe discharged. The solution drains from the sinus through the ostium maxillare (and accessory ostia, if any) into the nasal fossa and hence into an emesis basin held under the patient's nose.

It is not necessary to anesthetize the flap. No discomfort is experienced by the patient.

The solution used in this work usually has been 200,000 units of penicillin in 20 cc. of an isotonic salt solution. Sulf-Opto (Abbott) also has been used. As little as 3 cc. and as much as 13 cc. of this antibacterial agent has been injected at one treatment.

As a supplement to this treatment a nasal spray of the solution of penicillin in an isotonic salt solution has been prescribed sometimes. Three hundred thousand (300,000) units of penicillin in oil and wax always has been given by injection in the hip for several successive days after the irrigation.— *Edward H. Toler, D.D.S., Kansas City, Mo.*

UMI

THE IMPORTANCE OF BIOPSY IN ORAL DIAGNOSIS

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THE BIOPSY is an important adjunct in the diagnosis and evaluation of many oral lesions. Because of lack of an appreciation of its importance, and because it is considered to be a rather formidable procedure by some practitioners, it is not used as extensively as might be desirable.

The removal of tissue specimens for microscopic examination is simple, inexpensive and painless. This can be carried out with a minimum of time and effort as an office procedure.

All rational treatment is based on a thorough examination and accurate diagnosis. Quite often it is not possible to rely on the objective and subjective findings alone to establish a diagnosis. Frequently laboratory procedures are indispensable. This is especially true of the biopsy. It should be used wherever possible as an adjunct in the establishment of a diagnosis.

Regardless of the clinical experience of the operator, the biopsy should be included in the data used to establish the final diagnosis in all neoplastic diseases in the region of the mouth and in all conditions suspected of being neoplastic. The differential diagnosis of many oral lesions is confusing and the final answer often may be obtained only by examination of tissue under the microscope. The program of treatment of lesions such as malignancies, tuberculosis, syphilis, fungus and virus diseases and other infectious inflammatory processes, differs so greatly that one can not afford to make a mistake in diagnosis. Frequently a surgeon is embarrassed by doing extensive surgery for what has been considered a malignant disease only to find on postoperative examination that the lesion is not neoplastic. It is conversely dangerous to treat lesions as benign or innocuous when in reality they are malignant. Much valuable time may be lost in this way.

Methods of Obtaining Specimens

The purpose of the biopsy is simply to obtain tissue for microscopic examination. The methods of obtaining this material are as follows:

1. Incision
   a. By scalpel
   b. By electrocautery
   c. By high frequency cutting current
2. Punch biopsy
3. Curettage
4. Paracentesis—for the examination of fluids (ascites, pleural fluid and so forth) for tumor cells
5. By aspiration

Preparation of Specimen

The biopsy material usually is prepared by embedding in paraffin and cutting

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thin sections from this for staining. In certain instances when it is desirable to obtain an immediate opinion from the pathologist regarding the nature of the tissue, the frozen section is desirable. The frozen section is prepared by freezing the material in a small block, sectioning it immediately and staining without embedding in paraffin. The frozen section is ready for examination within five to ten minutes and offers the surgeon the benefit of obtaining an immediate diagnosis from the pathologist while the patient is still on the operating table. In most cases the report influences the judgment of the surgeon in regard to the treatment of the lesion. Diagnosis by frozen section generally is conceded to be much less accurate than with regularly prepared paraffin sections, but in most cases, particularly when the report is positive for malignancy, it offers a practical, accurate diagnosis.

From the standpoint of the pathologist, excision of the whole lesion provides the best specimen for examination. This should be done in all cases where a lesion is small and where a biopsy necessarily would take practically the entire lesion. When small lesions are noted, they should be excised totally and submitted for examination.

From the clinical standpoint, generally it is presumed to be safer to remove small sections for examination rather than large sections. Small bits of tissue usually will suffice for positive diagnosis. When the diagnosis is positive for neoplasm the biopsy may be considered to have been adequate. However, negative biopsy should not be taken as a conclusive diagnosis from small bits of tissue. If the diagnosis is negative when a lesion appears clinically to be malignant, biopsy should be repeated.

The incisional biopsy is the one most often used for lesions of the oral cavity. Removal of the section with a sharp blade is generally the method of choice. In highly vascular tumors, it may be desirable to use the cautery method in order to minimize the bleeding at the site of biopsy. The high frequency cutting knife is also useful in obtaining biopsy specimens, but both the cautery and high frequency cutting knife must be used cautiously so as not to destroy the specimen by dehydration or charring. These instruments should be limited in removal of tissue for biopsy to those sections that are large and in which the heat will not penetrate the center of the section.

The punch forceps is useful in removing small bits of tissue from inaccessible regions such as the maxillary sinus and lateral or posterior pharyngeal wall.

Curettage seldom is used in the biopsy of oral lesions because of their easy accessibility. However, it might be useful in removal of tissue from the depth of bony cavities, sinus tracts or the maxillary antrum. The material obtained by curet is embedded in paraffin and sectioned in the usual way. In some instances this may give sufficient tissue for diagnosis.

Paracentesis seldom is used in oral diagnosis. This is done by puncture and tapping of fluid from a body cavity. The fluid is centrifuged and the cells are embedded and stained in the usual manner for microscopic examination. This might well be used in examination of fluid from the maxillary sinus.

Aspiration is done with a large bore needle and a syringe or apparatus to provide negative pressure. The needle is passed into the suspected region, and by use of strong negative pressure fluid or cells are drawn into the lumen of the needle. The tissue is forced out of the syringe and is prepared for examination microscopically by embedding in paraffin, cutting and staining in the usual manner. This method is quite useful in examination of lymph nodes, cysts, tumors

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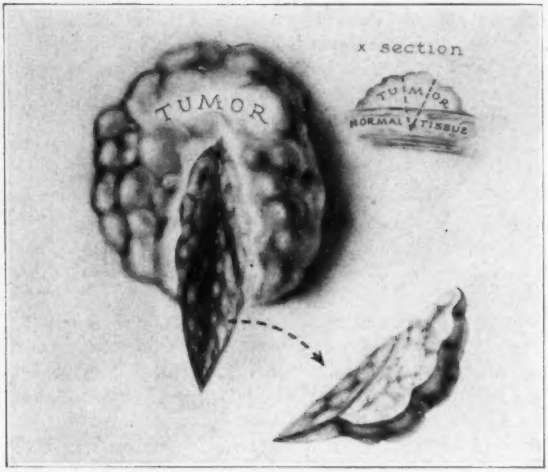

Drawing of biopsy section showing correct depth and shape of specimen. Normal as well as abnormal tissue should be included

and deeply located tissues that are not easily accessible by means of the usual incisional methods.

Dangers of Biopsy

It has been felt by some observers that the manipulation and trauma incidental to the removal of a section of tissue for biopsy might result in early metastasis of the tumor cells. But in the oral cavity the taking of a biopsy, if done with gentleness and care, need not be a matter of great concern as far as dissemination of the malignant tissue is concerned. It probably is much more dangerous to manipulate and palpate the tumor unnecessarily during the course of the examination.

It has been shown by some observers that the removal of tissue for biopsy does not increase the incidence of metastasis. Certainly the minimal dangers incident to the removal of a biopsy section are far outweighed by the dangers of attempting any type of treatment without a definite diagnosis. Under no circumstance should treatment of a neoplasm be attempted without a positive diagnosis by microscopic means whether the lesion is far advanced or in early stages of its development.

The lapse of time after the removal of the section for microscopic study and before surgery is instituted varies to some degree. In general it is much better to institute treatment within the earliest reasonable length of time following the excision of tissue for biopsy. In certain types of tumors, particularly those of the breast, bone and thyroid, a biopsy should not be done until the surgeon is ready to proceed immediately after examination of the frozen section if malignancy is found to be present.

Biopsies of the skin, lips, oral pharynx, uterus and bladder are less dangerous;

a reasonable length of time may elapse safely before treatment following the removal of tissue for biopsy. In any case where a melanoma is suspected, the biopsy should include the entire specimen; under no circumstance is it safe to cut into tumors of this type.

Selection of Sites for Biopsy

In providing the pathologist with adequate tissue for study, the following rules should be kept in mind:

1. A representative region is chosen from which the biopsy specimen is to be obtained. This should be the region of the lesion which in general represents the greater portion of the whole pathologic picture.

2. Thin, deep sections should be removed rather than broad, shallow sections. The broad, shallow, superficial section of tissue simply may show hyperkeratosis or inflammatory reaction without actually showing the presence or degree and extent of invasion of the tumor cells in the depth of the lesion.

3. Normal as well as abnormal tissue should be included in the biopsy specimen. In other words, a specimen should be taken through the margin of the lesion.

4. An elliptical shaped section generally is desirable. The cuts are made vertical to the plane of the mucosal surface or converging to give a *V* shaped section.

5. Crushing or mutilation of the specimen should be avoided. Special caution should be observed in handling the specimen with forceps.

6. Care should be taken not to include crust or sloughs from the lesion as biopsy specimens. These give inconclusive material for study and do not show representative sections of the neoplasm.

7. Specimens should be taken from more than one area of the tumor if it appears different in character in these regions. A small drawing of the lesion should be made, and each specimen should be placed in a separate bottle and labeled *1, 2, 3* and *4* to represent the area from which the specimen has been removed. If several specimens are taken from different lesions, each of these should be identified definitely and placed in a separate bottle with label attached.

8. All biopsies in the region of the oral cavity should be cut deeply in order to show basal tissues.

9. When electrocautery or a high frequency cutting knife is used, care should be taken not to destroy the character of the cells by heat or dehydration.

10. After removal of a section of tissue, it should be placed in a container in 10 per cent formalin solution (4 per cent formaldehyde). The section should be placed in the solution; under no circumstances should the section be placed in the dry container before application of the solution to it. This provides an opportunity, particularly with small sections, for dehydration of the tissue and sticking to the side of the container. The solution should be in the container and the specimen dropped into the solution.

11. In the case of small lesions, the entire lesion should be removed for study rather than a small portion of a small lesion.

12. All specimens should be labeled carefully and identified with the patient's name, address, occupation and age.

13. The pathologist should be provided with a short history of the development of the lesion and a brief statement of the locality from which the lesion

UMI

was obtained. Inadequate information makes it difficult and time consuming for the pathologist and may lead to an inaccurate evaluation of the material submitted.

If the material is taken in the surgeon's office it can be transported readily to the pathology laboratory by means of a small mailing tube. These are available from the pathology laboratories on request.

Benefit to Both Patient and Operator

All abnormal tissue removed from the region of the oral cavity should be submitted for examination. Quite often epuli, hypertrophic soft tissue, material from bone defects and so forth are found to contain highly significant pathology. For the benefit of the patient and for the protection of the surgeon, this information should be available. It should be a standing rule in every office and clinic that a section of all abnormal tissues be submitted for study.

Generally the permission to take a biopsy specimen is not difficult to obtain when the patient understands there is a possibility that some serious condition might exist. Most patients are intelligent enough to want to know the cause of the difficulty and will give permission readily for biopsy. This is particularly true if there is some question about the presence of malignancy.—*Department of Oral Surgery, University of Michigan.*

Survey of Pathologic Specimens from the Oral Regions Seen at the Army Institute of Pathology during World War II. Joseph L. Bernier, in *Mil. Surgeon* 101:362, 1947.

Fifteen cases of Ludwig's angina have been recorded, which indicates that, although rarely seen, the condition remains a problem because of its serious prognosis.

Only 3 cases of Mikulicz's disease were seen. The intensity of infiltration of lymphatic elements was a striking feature. The gland acini become widely separated and atrophic while the ducts undergo hypertrophy in this condition.

Leukoplakia can be classified histologically into two types: (1) the verrucal form, and (2) a leukoplakia which shows less keratotic activity and more widespread involvement. About three-fourths of the lesions reported were on the lips and of these, almost all occurred on the upper lip. Primary syphilitic lesions of the lip may grossly resemble the infiltrating type of carcinoma.

Oral tuberculosis occurs most frequently on the tongue, lips and pharynx, in the form of rough, motheaten ulcers which may resemble aphthous ulcers and squamous cell carcinoma. Histological differentiation from sarcoid is extremely difficult.

Because of confusion concerning the term epulis, its use has been discontinued. Peripheral giant cell tumors (giant cell epulis) arise from the periodontal membrane and have a high incidence of recurrence. Granuloma pyogenicum cannot be differentiated histologically from pregnancy tumors of the gums.

Of the 38 salivary gland mixed tumors which occurred on the lips, 35 occurred on the upper lip. Eight hundred and twenty-seven squamous cell carcinomas of the lip are recorded; they may be classified into papillary and ulcerating forms. One of every 5 specimens submitted to the Institute was malignant, and one of every 8 specimens was a squamous cell carcinoma of the lip. Certain factors peculiar to military existence may be responsible, such as excessive radiation, wind and dust.—John R. Lindsay, in International Abstracts of Surgery, *Surg., Gynec. & Obst.* 86:433 (May) 1948.

UMI

STUDIES IN BONE HEALING: STIMULATION OF HEALING IN LONG BONES BY USE OF ARTIFICIAL MATERIAL

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NEARLY ALL PROCEDURES of dentistry involve bone directly or indirectly. An understanding of this interesting tissue in its response to injury is of importance to all dentists and particularly to the oral surgeon. This knowledge should dominate many phases of his technic.

Literature

From early investigations to the present time, attempts to stimulate new bone to fill gaps produced in long bones have been carried out by using the radius of the dog. The canine radius is fused to the ulna at both ends. While slight movement is permitted when the radius is sectioned, the two divided ends are sufficiently rigid to make such experiments possible without splinting the leg.

Bancroft[1] and later Murray[2] studied bone repair. Murray removed 2 cm. of bone and periosteum from the radius of a series of dogs. He reported that if the section was not replaced, or if it was decalcified and replaced, a fibrous union always resulted. He further reported that if the bone was replaced intact, or if it was comminuted or boiled and replaced, bony union followed. Murray reported success in further experiments when he filled the gap with the pure chemicals, calcium carbonate and calcium phosphate. Shands[3] repeated Murray's experiments, using glycerine phosphate as a chemical stimulant, and reported success. Stewart,[4] in reporting a series of similar experiments, stated that he was unable to establish a bony union.

For years the question has been raised repeatedly as to the origin and function of cells called osteoblasts, while the existence of specific cells as such has been questioned. Some investigators have claimed that periosteum is the only tissue capable of furnishing the source from which new bone forms. Others deny this. In 1912, Macewen[5] described the chief function of periosteum as one of delimiting and controlling the direction of new bone growth. In one of his experiments he removed $1\frac{1}{8}$ inches from a dog's radius and fitted one of the cut ends of bone into a glass tube. He reported that part of the tube was filled with new bone in eight weeks and five days.

Leriche and Policard[6] state that the physiologic growth of new bone is inversely

This investigation was supported by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

1. Bancroft, F. W., Process of Bone Repair Following Trauma. *Am. J. M. Sc.* 147:809 (June) 1914.
2. Murray, C. R., Repair of Fractures. *Minnesota Med.* 13:137 (March) 1930.
3. Shands, A. R., Studies in Bone Formation; Effect of Local Presence of Calcium Salts on Osteogenesis. *J. Bone & Joint Surg.* 19:1065 (October) 1937.
4. Stewart, W. J., Experimental Bone Regeneration. *Surg., Gynec. & Obst.* 59:867 (December) 1934.
5. Macewen, Sir William, *Growth of Bone.* Glasgow: James Maclehose & Sons, 1912.
6. Leriche, R., and Policard, A.: *Physiology of Bone.* (Authorized English Translation). St. Louis: C. V. Mosby Company, 1928, p. 19.

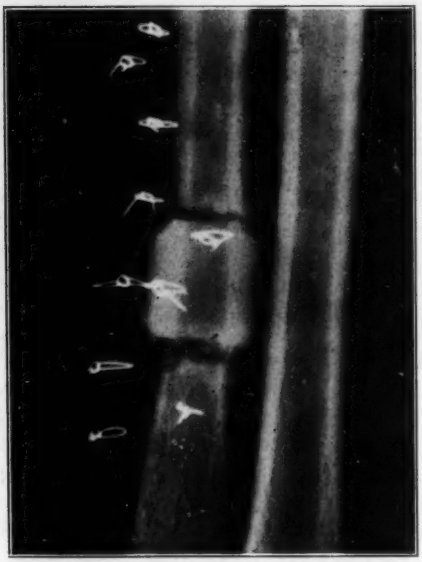

Fig. 1, Experiment 6.—Immediate postoperative roentgenogram showing satisfactory placing of implant

proportional to the differentiation of the connective tissue from which it is formed. It often is implied, and it is stated that a tissue in order to repair itself must revert back toward its embryonic origin. In the case of bone, its embryonic origin is primitive connective tissue. This tissue is formed in the initial blood clot which is present whenever bone injury occurs. The chemical theory of bone healing has been studied intensively by Robison[7] and others.

Purpose of Investigation

This investigation was undertaken to discover whether bony union would occur if 1 or 2 cm. of a dog's radius were removed with its periosteum, provided the following conditions were present:

1. That a blood clot, as the precursor of primitive connective tissue, was allowed to form between the two cut ends of bone.

2. That this clot was protected from invasion by surrounding differentiated tissue until calcification could take place.

To fulfill these conditions it seemed that a tube might be made and placed in the surgically prepared breach. A satisfactory tube for this purpose should be nonirritating to tissue and of such a nature that it would be removed from the healing region by tissue action. In the case of the dog it should be removed in a period of about two weeks. The possibility of the material from which the tube was made furnishing mineral salts directly to the region of healing was considered.

7. Robison, R., *Significance of Phosphoric Esters in Metabolism.* New York University Press, 1932, pp. 56-57.

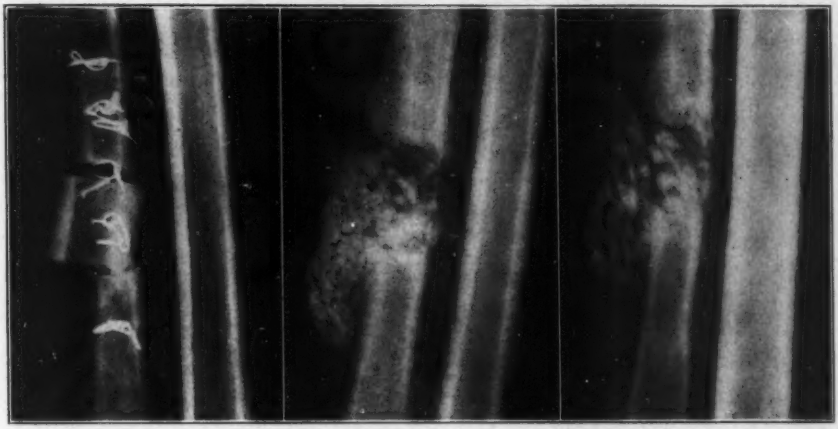

Fig. 2, Experiment 1.—Left: Immediate postoperative roentgenogram showing unsatisfactory placing of implant. Center: Forty-two days after operation showing preosseous material spilled into tissue. Right: Ninety-one days after operation showing formation of hard spur in operative region

Construction of Tube

In the construction of this tube a paste, similar to that used in earlier experiments,[8] was employed. A mixture of chemically pure salts, consisting of tricalcium phosphate 95 per cent, calcium carbonate 3 per cent, magnesium carbonate 1 per cent, sodium carbonate 0.5 per cent, calcium chloride 0.2 per cent, sodium chloride 0.2 per cent, and ferrous sulfate 0.1 per cent, was ground to a fine powder and mixed to a homogeneous mass. Ordinarily about 1 kg. of the salts was

8. Schram, W. R., and Fosdick, L. S., Studies in Bone Healing. *J. Oral Surg.* 1:191 (July) 1943.

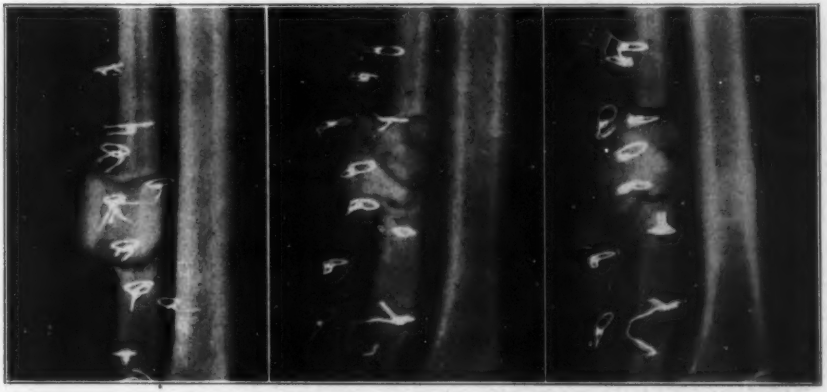

Fig. 3, Experiment 2.—Left: Immediate postoperative roentgenogram of relatively large implant fairly well placed. Center: Seven days after operation. Right: Twenty-one days after operation

UMI

prepared at one time. The powder then was divided into 25 Gm. lots, placed in clean, dry flasks and dry sterilized at 120 C. for two hours. A solution then was made by adding 5 per cent of U. S. P. gelatin to sterile distilled water. This solution was boiled gently for fifteen minutes. Evaporation was prevented by covering the mixture with a watch glass. Ten cubic centimeters of the gelatin solution then was blended with 10 Gm. of the previously prepared sterile bone salts. This mixture was forced into a sterile glass tube with suitable lumen to form the desired diameter for the implant. The tube was fitted with a sterile glass rod in order that the material might be extruded into a sterile weighing bottle. When the weight was determined, the material in its uncovered container was placed in a vacuum desiccator and dried until the water content of the intended implant was 3 per cent.

The size of the material used in these implants required a drying time of seven hours. The water content of the material seemed very critical. Several experiments were made with implants containing more or less moisture which produced unsatisfactory results. After the drying period the material was of about the consistency of chalk and was contoured easily to the desired shape. Under aseptic conditions a hole was drilled through the center to produce a tube. This was done shortly before operation. After the section of bone was removed from the radius, any further shaping of the material which was to be implanted was done with a scalpel.

Operation

The experimental animals were given Nembutal (Abbott) subcutaneously and, under surgical conditions, the radial bone was exposed. A bi-bevel drill was used to cut through the bone and periosteum in two places, a centimeter or two apart, and the severed piece of bone was lifted out. There was no means of being certain that all of the periosteum was removed by this operation, but every effort was made to do so. In addition, in several experiments which were made using identical technic for the surgery but placing no implant, a fibrous union always resulted. After the removal of the section of bone, a tube of the experimental material of suitable shape was placed in the breach. Two or three fine tantalum wire sutures were placed across the adjoining muscle sheaths to hold the material in place. The skin was closed with the same suture material. The leg was not splinted and the sutures were not removed since they did not seem to be antagonistic to healing. A suture occasionally was lost as repair took place.

Roentgenographic Study

Roentgenograms were made of each implant immediately following surgery and at approximately weekly intervals thereafter. The material used as an implant shows about the same density as does bone in these roentgenograms, and thus its position is demonstrated readily. The roentgenograms submitted all show radiuses of dogs which have had implants made of the material which was prepared as described and dried for seven hours in a desiccator.

Experiment 6 is recent, and only one roentgenogram (Fig. 1) taken immediately after surgery is shown. This is presented to illustrate what is believed to be satisfactory placing of the implant. In the experiments which were done there seemed to be some indication that if there is a small space between the

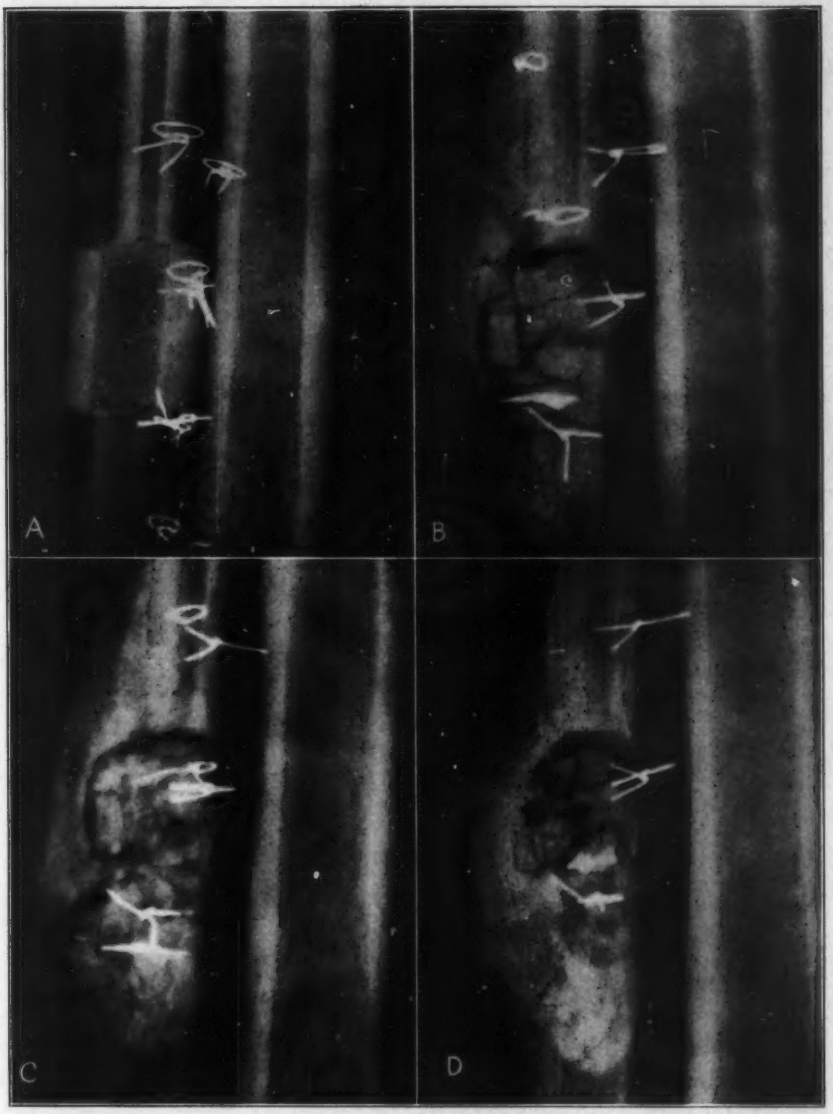

Fig. 4, Experiment 3.—A: Immediate postoperative roentgenogram of large implant in place in small radius. B: Twenty-eight days after operation. Radiopaque material on side of breach appeared to be callous type of bone growth. C: Thirty-six days after operation showing formation of what appeared to be a false joint. D: Seventy-one days after operation. A heavy bridge of bone appears to be uniting two ends of the radius

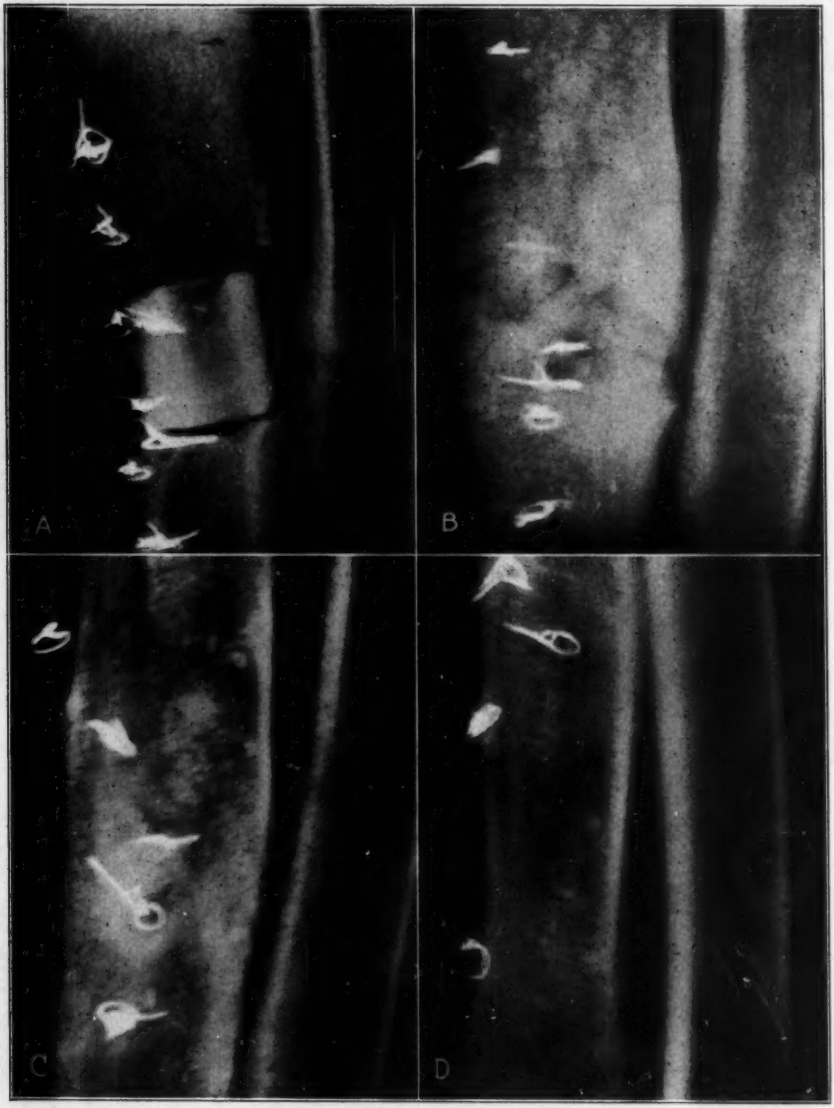

Fig. 5, Experiment 4.—A: Immediate postoperative roentgenogram of an unusually large radial bone. B: Twenty-one days after operation showing radiopaque material. C: Fifty-one days after operation. D: One hundred and twenty days after operation. Breach is filled completely and bone pattern is beginning to form

cut ends of bone and the implant, it is more likely to remain in good position. It is thought that the early displacement of some of the implants which were made may have been caused by the slight movement which is permitted the cut ends of the radius.

The immediate postoperative roentgenogram of experiment 1 (Fig. 2) shows that the position of the implant was not satisfactory, and it might be expected that if a preosseous material did form within its lumen, it would be spilled out into the tissue at the distal end. Roentgenograms taken forty-two days after the operation seem to indicate that this occurred. Ninety-two days after surgery, clinically there appeared to be a hard spur of considerable size on the bone in the region of operation. The overlying skin was healthy and freely movable. Roentgenograms taken at that time indicate that calcification is bridging the cut ends of the bone.

The roentgenogram taken immediately after the operation in experiment 2 (Fig. 3) shows a relatively large implant fairly well positioned. The one taken seven days later shows the breach in the bone filled with an amorphous mass which is difficult to identify. Twenty-one days after the operation no appreciable change was apparent. On this date the dog was sacrificed and the radiopaque material in the healing region, together with the surrounding bone, was removed and is being decalcified in preparation for histologic study.

The immediate postoperative roentgenogram of experiment 3 (Fig. 4) shows a large implant in place in a comparatively small radius. Twenty-eight days later there was little roentgenographic evidence that the material used as the implant remained in the region. There was considerable radiopaque material building up along one side of the breach. This appeared to be a callous type of bone growth. A roentgenogram taken thirty-six days after the operation showed more of the radiopaque material, and there was a suggestion that a false joint was being formed in the operated region. This again seems to indicate that slight movement is present in the cut ends of the radius. The last roentgenogram of this dog was taken seventy-one days after surgery. It shows what appears to be a heavy bridge of bone securely uniting the two ends of the radius. This dog will be kept for several months in order to observe what changes, if any, will take place in the radiopaque material as the leg functions.

The immediate postoperative roentgenogram of experiment 4 (Fig. 5) shows that the implant is well placed in an unusually large radial bone. Twenty-one days later an abundance of radiopaque material appeared within the region. Roentgenograms taken fifty-one and 120 days after the operation seemed to show the breach in the bone completely filled, and there was an indication that bone pattern was beginning to form.

When it became likely that a firm union was occurring in the radius shown in experiment 4, the other foreleg of the same dog was operated on (Fig. 6, experiment 5). This was the only instance in which an attempt was not made to remove all of the bone. The immediate postoperative roentgenogram shows a comparatively short implant in a radial bone which is large and is not cut completely through. Although not intentional, it was evident that the small fragment of bone left to connect the two cut ends of the radius was fractured. Roentgenograms taken fourteen days, twenty-two days and forty-seven days after surgery showed progressively the healing as it had taken place in the operated region. In this one experiment the work was done as outlined to avoid taking an unnecessary risk of nonunion in the second leg operated. The repair in the first leg

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to be operated had extended over a period of 120 days and is shown in the final roentgenogram of experiment 4 (Fig. 5). The healing of the second leg of this

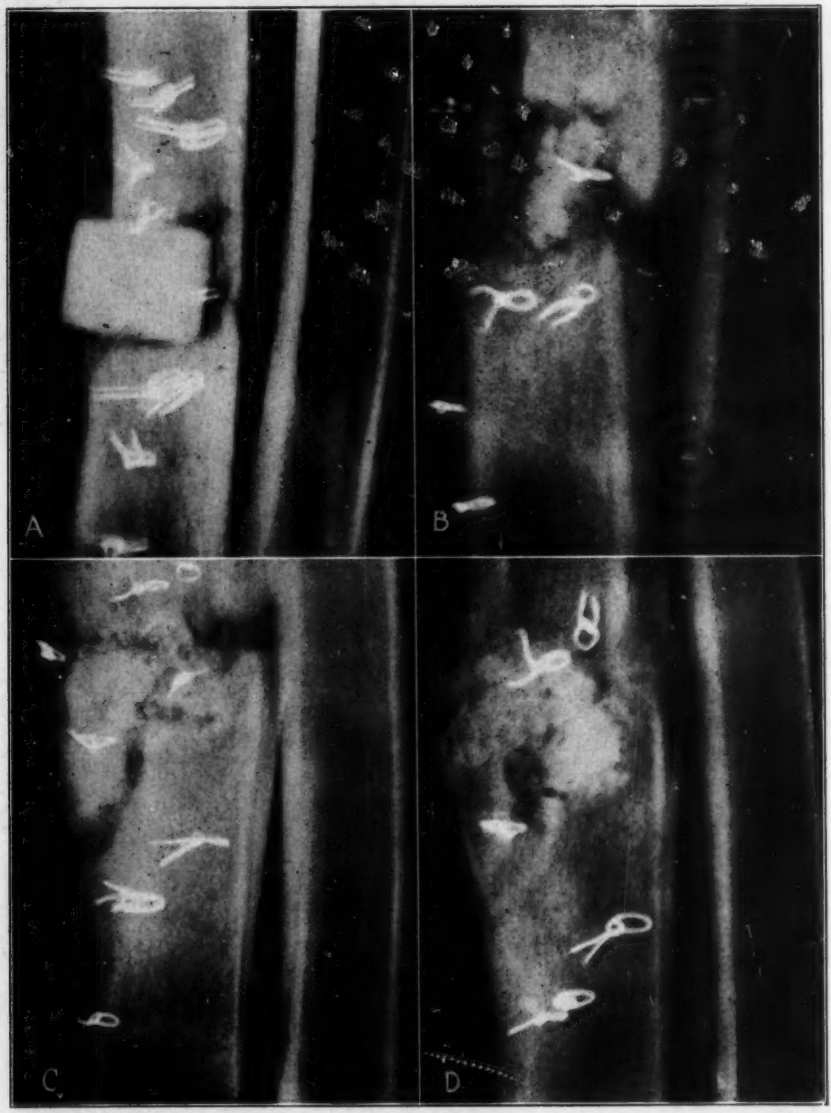

Fig. 6, Experiment 5.—A: Immediate postoperative roentgenogram of a short implant in a large radial bone not cut completely through. B: Fourteen days after operation. C: Twenty-two days after operation. D: Forty-two days after operation

dog extended over a period of forty-seven days and is shown in the final roentgenogram of experiment 5 (Fig. 6). The dog will be kept over a long period of time in order to study progressively any development of bone pattern as shown by the roentgenogram.

In addition to the experiments reported, a number of implants have been made recently and it is our intention to make more. All of these implants will be followed by periodic roentgenograms. At such time as seems proper the dogs will be sacrificed and the healing regions studied histologically.

Summary

When 1 cm. or more of the entire bone and periosteum is removed from the canine radius, fibrous union occurs if the space is untreated. When such a space is filled by a tube consisting of the mineral salts, as they are present in bone, in a gelatin matrix, roentgenographic evidence indicates that bony union occurs. This fact seems to support the premise that it is necessary to allow a blood clot to form between the two cut ends of the bone, and to protect the clot from the surrounding differentiated connective tissue, until calcification has taken place.—*311 East Chicago Avenue.*

The Chondrojet. E. Hoyt DeKleine, in *Plast. Reconstr. Surg.* 3:95, 1948.

The author describes a new instrument and technic which facilitates the handling of diced cartilage for reconstruction of contour defects of the face. Diced cartilage implies material chopped into 1 to 3 mm. multifaceted particles. Customary methods of burying this material require rather large incisions directly over the defect. This has cosmetic disadvantages, as well as increasing the likelihood of extrusion of cartilage fragments, bacterial contamination and increased operating time.

The chrondrojet consists of a straight steel tube with a syringe-type piston and finger grips, and a funnel and tamper for loading. Incisions are made a few centimeters from the recipient area, in inconspicuous places; a tunnel then is dissected to the recipient site, the loaded chondrojet is introduced through this tunnel, and its contents are extruded. After closing the incision, the cartilage mass is molded to a smooth contour, and pressure dressings are applied.

This method was carried out 17 times on 11 patients with gratifying results. The operating time was reduced over 50 per cent, no major infections were encountered, loss of cartilage fragments by extrusion was negligible, and scars were inconspicuous. Serum accumulations were frequent and were treated by aspiration. Locations and conditions included receding chins, malar and frontal depressions, depressed orbital floors and asymmetrical mandibles. Local anesthesia was used, and in all cases preserved rib cartilage implants were employed. It is the author's opinion that living cartilage grafts offer no advantages over preserved cartilage implants.—S. Lloyd Teitelman, in International Abstracts of Surgery, *Surg., Gynec. & Obst.* 86:605 (June) 1948.

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FIBROUS DYSPLASIA OF FACIAL BONES WITH REPORTS OF CASES

Alton K. Fisher, D.D.S.,
New Orleans

FIBROUS DYSPLASIA of bone gradually is being accepted as a distinct disease entity. It is becoming apparent that the condition is not rare although only the literature of the last decade contains any references to it. Its lesions undoubtedly have been observed previously but have been confused with or diagnosed as manifestations of hyperparathyroidism, connective tissue neoplasia, osteitis fibrosa, fibrous osteodystrophy, osteodystrophia fibrosa unilateralis, unilateral polyostotic osteitis fibrosa, unilateral Recklinghausen's disease, osteitis fibrosa disseminata, osteitis fibrosa cystica, Albright's disease, Paget's disease and Hand-Schuller-Christian disease. Probably there are many instances, not necessarily recorded, in which the solitary lesions mistakenly have been identified as being associated with other more commonly recognized pathologic processes.

Literature

In 1933 Jaffe expressed the opinion that certain skeletal lesions which had been attributed to hyperparathyroidism were possibly those of a still unidentified pathologic entity, and he suspected that it had a congenital basis.

Jaffe's observations stimulated a detailed investigation of the problem by Lichtenstein. The results of his study were presented in 1938, under the title of "Polyostotic Fibrous Dysplasia."[1] Lichtenstein described the clinical features of the disease and correlated them with the characteristics of the lesions. He was unable to explain its etiology but he offered a concept of its pathogenesis.

In order to eliminate confusion and ambiguity, he refrained from designating the disease by one of the baffling array of older terms which might have been applicable and introduced a new term which was descriptive of the process involved. He used the term polyostotic fibrous dysplasia "to designate a skeletal developmental anomaly affecting several or many bones with predominantly unilateral involvement. The involved bones show filling of their medullary cavities by gritty, grayish white fibrous tissue containing trabeculae of newly formed primitive bone. The condition apparently results from perverted activity of the specific bone-forming mesenchyme. It manifests itself in childhood or early adult life and evolves slowly, pursuing a protracted clinical course characterized by pain, deformity and a tendency to pathological fracture of the affected bones." Lichtenstein's paper was based on the study of a small series of cases, but the investigations were sufficiently thorough to justify the identification of fibrous dysplasia as a distinct disease entity.

A definitive paper by Lichtenstein and Jaffe on fibrous dysplasia of bone was published in 1942.[2] Their experience with the subject had been expanded greatly through the study of a much larger series of cases than that which formed the

Professor of pathology, School of Dentistry, Loyola University, New Orleans.
Photomicrographs prepared by James B. Arey, Department of Pathology, Tulane University Medical School.
1. Lichtenstein, Louis, Polyostotic Fibrous Dysplasia. *Arch. Surg.* 36:874 (May) 1938.
2. Lichtenstein, Louis, and Jaffe, H. L., Fibrous Dysplasia of Bone. *Arch. Path.* 33:777 (June) 1942.

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basis for Lichtenstein's earlier paper. The conclusions drawn from the previous study were not changed significantly by the results of the second, but they assumed greater validity when supported by the augmented data. In the earlier paper fibrous dysplasia of bone seemed to be considered as essentially a polyostotic disease, and it was suggested that its monostotic occurrence was perhaps a more limited manifestation of it.

However, in the later paper the authors concluded that it was a pathologic entity in which "one, several or many bones may be implicated." The same process which produces the solitary monostotic lesion is considered to be active in producing the multiple polyostotic lesions, and the latter are regarded as a more florid expression of the fundamental disease. Since the publication of these two papers by Lichtenstein and Jaffe, additional articles have appeared by other authors on the subject of fibrous dysplasia of bone, but most, if not all, have been confined to a consideration of the polyostotic variety.

It is the purpose of this paper to direct attention to this seldom recognized disease and to enumerate those characteristics by which its diagnosis may be established. An attempt is made to explain the more proximate processes by which the lesions of fibrous dysplasia of bone are produced so that the diagnostic findings may be made more understandable. No effort is made to consider in detail the systemic abnormalities which, in some cases, may be associated with this disease, for this is done quite extensively in most of the literature on the subject. As a contribution to the slowly growing fund of information on the subject of fibrous dysplasia of bone, the salient features of 3 previously unreported cases of the monostotic variety of the disease are presented.

Pathogenesis

The etiology of the disease is still unknown. Pathogenetically it appears to result from anomalous development of the bone-forming mesenchyma. The multipotent mesenchyma, instead of fulfilling the function of normal bone formation, proceeds to the production of localized masses of fibrous connective tissue. This aberrant mass of tissue may be composed largely of cells which appear more spindle-shaped than stellate and which are arranged in closely adjacent whorls, or it may consist predominantly of collagenous fibers. Some lesions show all gradations between and including these extremes. Particularly in the more cellular regions thin-walled vessels are not uncommon.

That the mesenchyma from which this tissue is derived has not lost completely its capacity for osteogenetic differentiation is indicated by the presence throughout the tissue mass of irregular bone spicules in various stages of development. These trabeculae do not seem to be oriented in a functional pattern but appear to be scattered rather purposelessly. They are more abundant in vascular and cellular regions than in those which are more obviously fibrous. Few or many giant cells may be present. These cells are usually small, containing less than a dozen nuclei, and apparently are produced by metaplasia of the basic tissue. In some regions, at least, these multinucleated cells are osteoclastic, although this relationship is not demonstrable in the great majority of their occurrences. Some sections may show a confused picture of osteogenesis and osteoclasis. Masses of cartilage also may develop through metaplasia. Some regions of the dysplastic mass may undergo cystic degeneration, although the exact mechanism by which this is accomplished has not been established definitely.

The lesion originates in the medullary spaces of the bone. As the dysplastic tissue proliferates, it replaces the medullary substance and eventually encroaches on the cortical bone. The thinning bone cortex is expanded gradually by the slowly enlarging mass contained within it, thus producing a bulging type of deformity. Should this process occur in a bone which is subjected regularly to appreciable loading, the inability to withstand the applied forces often results in a deformity which is distinct from, but combined with, that caused by local expansion. Pathologic fracture is a frequent clinical feature of the disease.

There are certain aspects of fibrous dysplasia of bone which simulate neoplasia. Indeed, there are several instances cited in the literature of lesions which were diagnosed as tumors of connective tissue, but a study of the clinical and microscopic findings in these cases revealed many features common to fibrous dysplasia. The abnormal structure of the lesion, coupled with the absence of characteristic inflammatory changes and the slow, expansive growth which is uncorrelated with the requirements of the organ in which it is contained, and which it may ultimately destroy, certainly are traits common to many so-called benign neoplasms.

Lichtenstein and Jaffe state, "In a sense, the individual bone lesion may be conceived as a hamartoma—i.e., a tumor-like malformation resulting from flaws of development and characterized by defects of tissue combination." Our present concepts of neoplastic disease do not always permit a rigid and entirely accurate disposition of certain tissue changes into neoplastic and non-neoplastic categories. This disease may be a representative of that group located at the dividing line of the two categories. It is important to note that no case has been reported

Fig. 1, Case 2.—Intra-oral roentgenogram of maxilla of a 19 year old Negro man, showing fibrous dysplasia. Note the irregularly cloudy appearance of the radiolucent area in the cuspid and bicuspid region. Bone trabeculae are most apparent just mesial to the roots of the first molar

yet in which a fibrous dysplastic lesion of bone has been transformed into a malignant neoplasm. On the basis of existing definitions and classification systems, and still inadequate understanding, it probably is not justified to consider fibrous dysplasia of bone as a form of neoplasia in the usually accepted meaning.

Diagnosis

The development of the lesions is slow and may begin in early life. They may be single or multiple, may be confined to a single bone or may be present in many. Where several bones are involved, the distribution is predominantly unilateral.

With the extensively involved cases developing in early life, certain extraskeletal manifestations may be associated. These include abnormal pigmentation of the skin, often in a blotchy pattern, and precocious sexual development in females. This latter feature may be accompanied by premature skeletal maturation. Glandular dysfunction does not seem to be a consistent finding. Pain may or may not be an accompaniment of the disease and possibly is related to the degree of involvement and to the nature of the functions of structures involved.

The most obvious objective symptom in well defined cases is expansion of the bone in the region of the lesion. Since the surface bone is still intact, the examiner may suspect he is palpating an osteoma. Questioning the patient at the time the swelling first becomes noticeable may be fruitless unless one bears

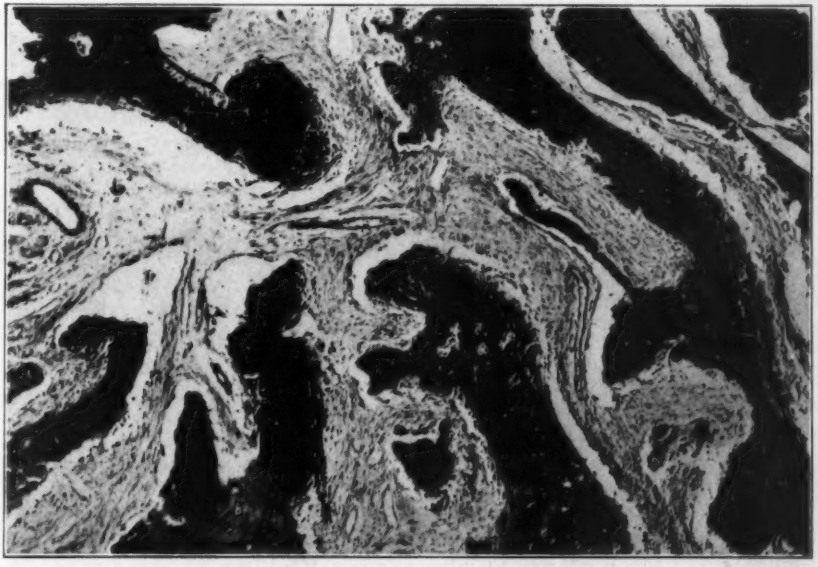

Fig. 2, Case 2.—Tissue section of surgical specimen obtained from fibrous dysplastic region of maxilla of a 19 year old Negro man. The large, irregular, elongated dark tissue masses extending in from the margins of the field are bone trabeculae. The intervening, lighter tissue is predominantly a moderately mature variety of collagenous connective tissue

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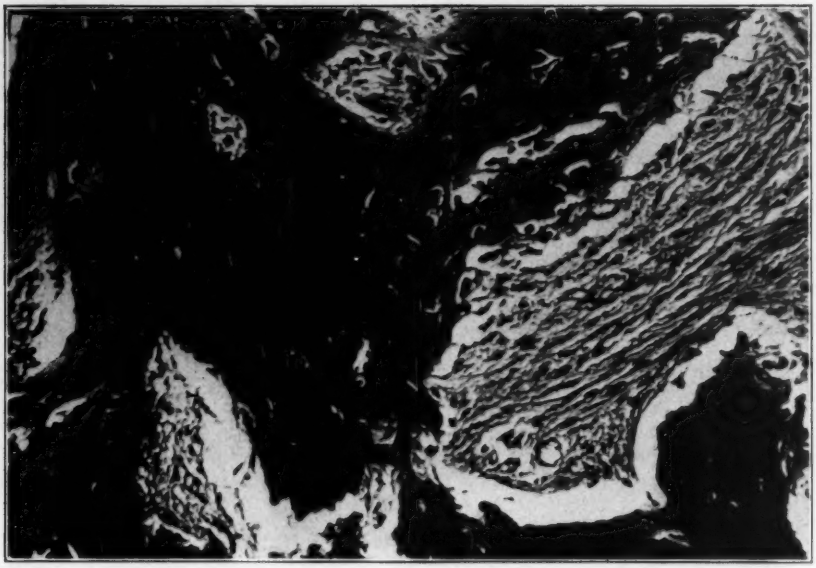

Fig. 3, Case 2.—Higher magnification of tissue shown in Figure 2. The predominating darkly stained tissue is bone. The lighter tissue extending diagonally into the field is fibrous connective tissue. Its capacity to approach maturity is indicated by its fibrous appearance and by the reduced volume and elongated outline of most of its individual nuclei

in mind the slow growth of these lesions which would make early subjective recognition of them difficult.

Roentgenographic Interpretation

Careful roentgenographic study is of great value in arriving at a correct diagnosis. Films must be exposed properly and processed accurately if the necessary tissue detail is to be recorded. They must be subjected to a discriminating examination in order to differentiate between the bone changes of fibrous dysplasia and other pathologic conditions, all of which may possess certain roentgenographic features of superficial similarity. The casual observer is led into error by his lack of appreciation of this fact.

The lesions of fibrous dysplasia result in bone destruction which is manifested by increased radiolucency. This is also the case in many neoplasms developing in bone, in inflammatory conditions, in cysts and in certain other pathologic states. The bone rarefaction, as shown roentgenographically, in the case of fibrous dysplasia, however, is not as diffuse as that usually produced by inflammatory processes.

On the other hand, the area of radiolucence is not delimited as sharply as in the case of static cysts. Static cysts are mentioned because it must be borne in mind that the bone cavities associated with growing and regressing cysts are characterized, respectively, by osteoclastic and osteogenetic activity; hence their

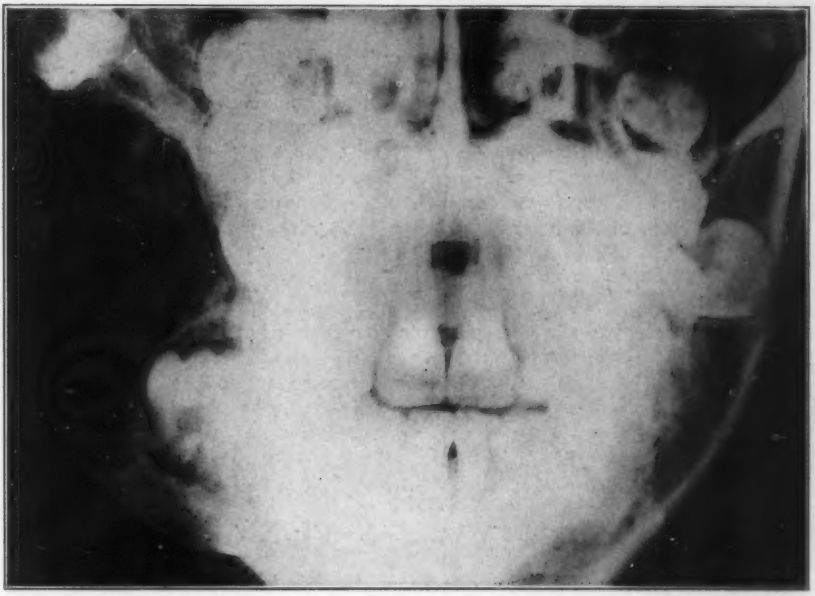

Fig. 4, Case 3.—Anteroposterior roentgenogram of face of 12 year old Negro boy. Note the laterally displaced right second molar and the superiorly displaced third molar crown well up in the ramus of the mandible. Compare the thin, distended cortical bone of this region with the normal left half of the mandible. The dysplastic region, while normally radiolucent, is irregularly cloudy and is traversed by scattered and incomplete septa

roentgenographic outlines will appear less distinct. Either of the two conditions may be confused with those of fibrous dysplasia.

However, if the microscopic features of the disease are remembered much of this latter confusion may be eliminated. The lesions of fibrous dysplasia do not appear as radiolucent as the usual cyst because they are composed of a denser mass of tissue. The small trabeculae of bone scattered throughout the mass contribute to its greater radiopacity and produce a more hazy appearance of the region of rarefaction. Larger trabeculae and bands of trabeculae may produce a slightly lacy pattern, and there are times when the lesion seems to be divided by numerous incomplete septa of rather delicate structure. All of these details may escape detection in a hurried examination of the film or fail to be recorded by poor roentgenographic technic. A combination of both of these possibilities can make a roentgenographic diagnosis almost worthless.

If a lesion suggestive of fibrous dysplasia is detected it will be helpful to examine other parts of the skeleton roentgenographically. The presence of similar lesions in other bones and in unilateral distribution is contributory evidence. However, the absence of other lesions does not rule out a possibility of fibrous dysplasia since it may be a monostotic as well as a polyostotic disease. Conclusive evidence eventually must be obtained from the microscopic examination of biopsy specimens.

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Tissue Examination

If surgical intervention is required, as in the removal of biopsy specimens or for other reasons, the removal of the cortical bone usually is achieved without difficulty. The tissue which fills the cavity in the bone is moderately firm, having a rubbery consistency. This is due to the predominance of fibrous connective tissue. A gritty sensation may be produced when the tissue is cut, and small pieces of it, when rolled between the fingers, may feel somewhat granular. The presence of small bone trabeculae in the tissue is responsible for these characteristics. The color of the mass is gray or grayish white with occasional small red dots.

Treatment

Since the etiology of the disease is unknown, a strictly rational form of therapy has not been established yet. Attempts to devise specific therapeutic procedures so far have not been successful. In a few cases roentgenotherapy has achieved only increased bone destruction. Surgery has been employed with varying results. When a lesion is exposed for biopsy, complete enucleation of the dysplastic tissue by curettage probably is justified. Whether or not the patient will benefit from the deliberate surgical removal of inconspicuous and uncomplicating lesions remains to be demonstrated.

The larger and more active lesions which endanger the near-future function of the bone present a different problem. The surgeon must decide between permitting the lesion to pursue its course and surgical intervention with its great risk of failure. Surgical treatment even of the large lesions has not proved to be effective on the whole. Repair of the bone defect with the aid of autogenous bone chips has yielded mixed results. Some lesions have recurred after curettage. There is a possibility that the smaller lesions which are not of immediate danger to the bone may become quiescent.

Report of Cases

Three cases of fibrous dysplasia of facial bones recently have come under the writer's observation.

Case 1

The face of an 11 year old white boy was deformed by an enlargement of the left side of his lower jaw. Except for this lesion, his history and physical findings were essentially negative. He complained of no symptoms, could give no definite information regarding the onset of the swelling and he appeared quite unconcerned about the deformity.

Examination.—On palpation the mass felt like bone and was confined to the lateral surface and inferior border of the mandible between the bicuspid region and the angle. The deformity did not disturb the occlusion of the teeth, and the alveolar process was not expanded palpably.

Roentgenographic examination had been requested, and the report suggested that the findings were compatible with chondrosarcoma. On the basis of this report a mandibular resection was contemplated.

In view of the drastic nature of the proposed treatment it was urged strongly that a biopsy examination be made before surgical intervention was attempted. This was done, the specimen being removed from the superior surface of the mass by an intra-oral approach.

Diagnosis.—The microscopic appearance of the tissue was quite characteristic of fibrous dysplasia. The specimens examined were predominantly fibrous and contained numerous trabeculae of bone. With the diagnosis established no further treatment was recommended. The case was examined periodically for a year thereafter, and no discernible change in the lesion was observed.

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Case 2

A 19 year old Negro man complained of a swelling in the upper right jaw. His history and physical examination revealed nothing of significance, and he could give no reliable information as to when the swelling first had appeared.

Examination.—The deformity consisted of a smoothly rounded, broad ridge of bone above the junction of the alveolar process with the body of the maxilla and extended from immediately posterior to the canine eminence posteriorly well into the molar region. This ridge, about 25 mm. in supero-inferior diameter, merged gradually with the surrounding normal bone surfaces.

Intra-oral roentgenograms showed localized regions of radiolucence which appeared adjacent to the apices of the bicuspid and molar teeth (Fig. 1). The case was diagnosed as multiple radicular cysts. However, the radiolucent regions appeared more indistinct and hazy than do the usual cysts, and the teeth in the region were not carious.

A biopsy was recommended, but this was not done because it was felt that the roentgenographic evidence for a diagnosis of radicular cysts was sufficiently obvious not to require further confirmation.

Operation.—The bicuspid and first molar teeth were extracted on the assumption that the apical vessels and nerves would be damaged irreparably in the removal of the cysts. A mucoperiosteal flap then was elevated, and the cortical bone of the abnormal mass was removed. This exposed what was described as "grayish, soft, necrotic bone" which was removed with a curet.

Diagnosis.—Microscopic examination of the surgical specimens showed the typical features of the collagenized variety of fibrous dysplasia of bone (Figs. 2 and 3).

Case 3

A 12 year old Negro boy appeared to be in excellent health except for an extensive swelling

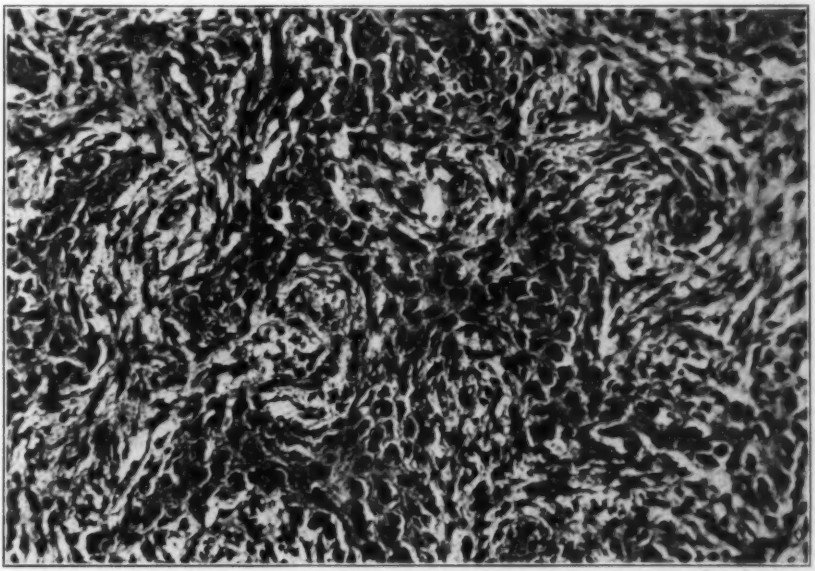

Fig. 5, Case 3.—Tissue section obtained from a region of fibrous dysplasia in the mandible of a 12 year old Negro boy. Lack of maturing or differentiating capacity is indicated by the juvenile morphologic character of the cells. Note the large volume of the nucleus and the relative absence of fibers

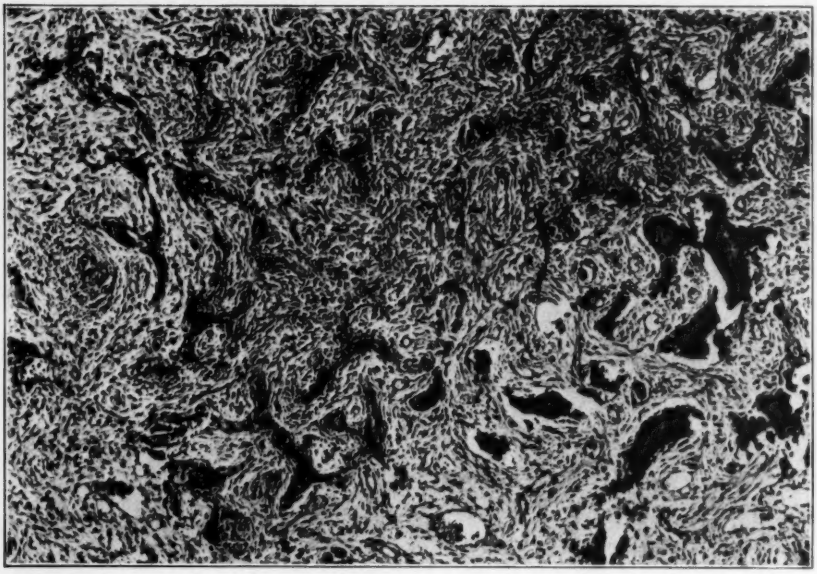

Fig. 6, Case 3.—Lower magnification of tissue shown in Figure 5. Note the highly cellular quality and the tendency toward whorl-like configuration. The dark masses are islands of bone formation. Several vessels can be seen which appear to consist of little else than an endothelial wall

of the right side of the lower jaw with which no symptoms of discomfort had been associated. As in the other cases, the development of the lesion had been evidently very slow, as no reliable information could be obtained as to when it first had become apparent.

Examination.—By palpation it was determined that the mass was bony and was associated with the lateral surface and inferior border of the molar region of the body and almost all of the lateral surface of the ramus of the mandible. Those teeth which had erupted were in normal occlusion. The alveolar process in the region of the unerupted lower right second and third molars was expanded laterally.

Roentgenographic examination showed the second molar to be depressed as compared to its normal position in the twelfth year, and it also was displaced laterally for a distance equal to its buccolingual diameter. The third molar was located almost as high as the mandibular notch and within the substance of the ramus. The entire structure of the mandible between these two teeth was expanded markedly and was quite radiolucent. Small irregular trabeculae and bony septa were demonstrable roentgenographically (Fig. 4). The case was diagnosed tentatively as possible multiple follicular cysts, possible ameloblastoma and as possible chondrosarcoma.

Operation.—The patient was subjected to surgery in which an external incision was made along the posterior border of the ramus and the inferior border of the body of the mandible. The soft tissue was retracted, and the thin cortical bone which formed the lateral wall of the abnormal mass was removed. The region was not cystic but was filled with not too firm a mass of tissue which was enucleated readily along with the two displaced teeth. Histologic examination of this tissue showed it to be composed largely of a highly cellular type of connective tissue (Fig. 5) in which the cells were found frequently to be arranged in a loose, whorl-like configuration. Small, thin-walled blood vessels were common. There were numerous trabeculae of bone, but these were not as prominent as in the other two cases.

Diagnosis.—Small giant-cells were not rare, and in some regions their presence was conspicuous.

The latter feature might lead one to make a diagnosis of giant-cell tumor of bone. The over-all character of the lesion, however, was typical of fibrous dysplasia of bone. (Fig. 6).

Summary

Fibrous dysplasia of bone is a recently identified disease which results in single or multiple lesions in one or many bones. The lesions in a single individual tend to be distributed unilaterally. They seem to arise from a developmental defect in the bone-forming mesenchyma which produces connective tissue masses with incomplete and varying osteogenic capacities. This pathologic tissue proliferates slowly and encroaches on the medullary substance and eventually on the bone itself, resulting in deformity and often in fracture. This disease may resemble several other pathologic conditions of bone in many of its characteristics but may be differentiated from them by careful consideration of its several peculiarities. Several cases of fibrous dysplasia of bone manifested by single lesions in the maxilla or mandible have been reported previously by Lichtenstein and Jaffe. This paper presents the salient features of 3 additional case reports. The etiology of the disease is unknown, and specific therapy is not yet established. Surgery has been employed with varying results—*6363 St. Charles Avenue.*

AMERICAN COLLEGE OF SURGEONS APPROVES USE OF NURSE ANESTHETISTS

The Board of Regents of the American College of Surgeons, at a meeting on February 22, 1948, adopted a resolution commending the services of nurses who have had special training in the administration of anesthesia and recommending the continuance of training courses in this field for nurses. The resolution reads as follows:

The American College of Surgeons regards with deep concern the actions of some physician anesthesiologists in giving the impression to the laity in the public press that it is unsafe for experienced nurse anesthetists to conduct surgical anesthesia. While it supports the increasing tendency of having physician anesthesiologists in charge of surgical anesthesia, it deplores at this time any propaganda for the elimination of the trained nurse anesthetist. On the contrary, the American College of Surgeons is of the opinion that, in view of the inadequacy in number of the physician anesthesiologists and in view of the splendid record of achievement of the nurse anesthetists, institutions engaged in the training of nurses for this purpose should be encouraged to continue their programs.

In its *Manual of Hospital Standardization* the American College of Surgeons states with respect to personnel in the Department of Anesthesia:

"The personnel in the Department of Anesthesia must consist of trained, competent assistants. Nurse anesthetists who have specialized in the administration of anesthetics are usually competent and acceptable for the work, but since they are not physicians licensed to administer drugs, they should be under medical supervision. If it is impossible to obtain or maintain a specially trained anesthetist in the community, a member of the medical staff who has had experience in anesthesia might assume the responsibility for supervision and direction of the department of anesthesia."—*Surgery, Gynecology and Obstetrics, June, 1948.*

UMI

TIC DOULOUREUX: TREATMENT AND DIETARY CONTROL

George M. Prince, D.D.S.,
Pasadena, Calif.

THE FIFTH NERVE, or the trigeminus, is subject to two types of neuralgia: (1) symptomatic pain, by far the most common, and (2) spasmodic pain, major trigeminal neuralgia or tic douloureux. Both types may involve any or all of the branches of the trigeminus, but the branches most frequently affected are the supra-orbital, infra-orbital, superior alveolar, inferior alveolar and mental. Of these, the second or third division is affected most commonly, followed in frequency by a mixed form involving several branches.

Functions of Fifth Cranial Nerve

The fifth cranial nerve is distributed extensively, transmitting sensation from the face, conjunctiva, nose, frontal and maxillary sinuses, teeth, palate, tongue, part of the upper pharynx and the scalp as far back as the vertex and the external auditory meatus; it transmits sensation from three quarters of the dura mater, falx cerebri and probably the tentorium cerebelli. In addition to carrying sensation from the above regions, the trigeminus supplies them with trophic, vasomotor and secretory fibers. The vasomotor fibers are brought to it in part from the medulla and cervical spinal cord by way of the sympathetic nerve. The secretory fibers have the same origin. The trigeminal nerve likewise innervates the muscles of mastication. The sensory part of the nerve is subject to sensory neurosis such as neuralgia, paresthesia and anesthesia.

Major trigeminal neuralgia is related closely to dental practice by virtue of its possible etiologic factors, its diagnostic relationships and the location of the terminal reflex neuralgia since these may be directly connected with dental lesions. The complex problem of diagnosis and treatment of trigeminal neuralgia is essentially one which concerns the oral surgeon.

Pain may be produced either by a distant or local cause. For example, an irritated or exposed pulp may cause pain in its immediate region and, as the nerves supplying the dental pulps are the peripheral endings of the large trunk through which pain impulses are transmitted, the pain may be referred to a distant point or other peripheral endings of the same or other trunks, manifesting itself as neuralgia in the ear, occipital headache and so forth because of the direct relation of the surrounding parts.

It should be remembered that the region of referred pain is not sensitive to pressure if the pain actually is referred, but if it is of local origin the tissues in the immediate region are tender to pressure.

Referred Pain

Referred pain can be caused by pressure, injury, trauma or irritation of the sensory nerves at a distant point. This stimulation is transmitted over certain sensory nerve branches to a remote part and interpreted there as pain. A good

Read at the staff meeting of St. Lukes Hospital, Pasadena, on January 15, 1948.

example is the experiment of touching the face, striking the teeth, cheek, or jaw, thus many times producing severe paroxysms of pain at some distant point. Another common example of referred pain which undoubtedly has been noted by many dentists is an instance in which the patient complains of pain in a specific tooth; on examination it will be found that this tooth is perfectly healthy and free from caries or irritation and instead a large carious cavity is present in the opposite jaw, the pain being referred by the connecting nerve branches. When proper treatment is employed the patient is relieved. Many times it is difficult to convince the patient that the pain is not located in the tooth in which no pathology is present. Another striking example of referred pain is the neuralgia which manifests itself in the ear, caused by a carious tooth located in either the upper or lower jaw. The pain is produced in the ear through the relation of the auriculotemporal nerve to the third or mandibular branch.

For a decade or more attention has been directed to the importance of temporomandibular joint disabilities in relation to pain showing marked variations in character in the regions of distribution of the fifth cranial nerve. The spectacular relief of symptoms afforded by occlusal splints or other measures that effect a lowering and forward positioning of the head of the condyle led to the assumption that direct pressure or traumatism of the trunk of the auriculotemporal nerve was the cause of the referred pains. Direct traumatism of the nerve trunk is considered to be impossible by anatomists. The referred pain must be caused by constantly recurring irritation of the joint structures including the meniscus cartilage by the movements of the condyle head in its acquired position of retrusion and upward displacement.

Severe and bizarre symptomatic pain in the facial region may be caused by disturbances of the histamine balance. In cases where no local cause of referred pain is discovered or where a possible cause has been eradicated without relief of symptoms, the patient should be referred for histamine studies and antihistamine therapy when indicated.

Diagnosis

In the diagnosis and treatment of patients suffering from tic douloureux, a thorough, careful examination should be made and all modern methods of diagnosis utilized. In the differential diagnosis one must consider such diseases as pulpitis, caries, chronic or acute alveolar abscess, lateral abscess, erosion, abrasion, exposed dentin, improperly placed fillings, pulp stones, temporomandibular joint arthrosis, empyema of the antrum and sinusitis. If all these can be ruled out trigeminal neuralgia then must be considered because it is a disease in which there is no definite etiologic agent. However, if the cause can be determined, then definitive treatment is given with the object of improving the condition or permanently eradicating the cause.

One must never lose sight of the fact that the cause of true tic douloureux is as yet unknown. Therefore oral surgical procedures undertaken in the hope that the condition is a pseudo-tic of referred origin should be based on adequate indications for surgery irrespective of the symptoms. This concept and plan of management should be explained thoroughly to the patient.

Many teeth are lost by improper or tardy diagnosis of tic douloureux. A frontal headache may be caused by a carious tooth, infection of the antrum, pulp stones, alveolar abscess, eye strain and so forth. To determine the etiology of referred

UMI

pain, the operator must be a diagnostician and search for the direct cause by careful physical examination and by the process of elimination.

In many instances nerve trunks have been blocked by alcohol to give the patient relief from pain when the real cause of the pain had been overlooked by the operator, and which, if located and treated, would have obviated the necessity for deep nerve block injection.

There is no pain quite as severe and agonizing as that of major trigeminal neuralgia or tic douloureux. In mild cases the patient may suffer only intermittently, sometimes going for days, weeks and even months without an attack, yet without a moment's warning the patient may be seized with a severe attack. In the severe types of cases, the pain may be agonizing and so frequent that it is practically continuous and in many instances associated with spasmodic contraction of facial musculature. Many of these patients have undergone every known medical treatment with little or no success resulting. It is extremely important to differentiate between the following described forms of trigeminal neuralgia.

1. Peripheral type—distal to ganglion
2. The ganglionic type
3. The retroganglionic or intracranial, reflex type caused by growths, tumors, cortical lesions and so forth
4. Symptomatic pains caused by other lesions which yield to local treatment

True tic douloureux occurs in middle or advanced life, and it is usually very severe in its symptoms and obstinate in its course. It always should be distinguished from the minor or symptomatic form of trigeminal neuralgia. Tic douloureux is probably due either to a toxic or to an atrophic process of nutritional or unknown origin which exists at some point in the various nerve branches, Gasserian ganglion or brain. A low grade neuritis which may be caused by infection such as an alveolar abscess, empyema of the antrum or an impacted third molar with infection, does not show changes in the nerve or branch, as a rule; but the small arteries which supply the nerves are bound to undergo endarteritis which causes their calibers to decrease and prevents the nerve from receiving its proper nourishment. In these cases the operation for an incisional removal of nerve trunk itself eliminates pain. In some cases the Gasserian ganglion has shown degenerative changes, but these have been considered purely secondary. These degenerative changes have not been proved to be the causative factor of tic douloureux as yet. Histologically the nerve has not been shown to possess any degenerative changes which would be characteristic of this disease.

Differential diagnosis must be made from pain caused by pulpitis, pus infection, impacted or carious teeth, or from a malignant growth. If the surgeon takes a careful history of the case and is very observing, he will note that the pain which arises from these factors is different from the pain present in a true tic douloureux. If the pain is paroxysmal in character, attacking the patient suddenly in one or more circumscribed areas situated over definite sensory nerve branch or branches, and persistently returns in a few hours, days or months in the same area, it is a case of tic douloureux.

Another characteristic of the pain experienced in tic douloureux is the presence of a trigger zone; that is, slight stimulation of a certain region on the skin or mucous membrane invariably reproduces the identical pain in the circumscribed region mentioned above. In making a diagnosis one should remember that a

UMI

hysterical facial pain frequently is mistaken for tic douloureux. In many cases where a mistaken diagnosis has been made, a nerve resection or an alcoholic injection may relieve the pain but does not remove the primary cause of the trouble.

Treatment

In major trigeminal neuralgia where no cause is evident, treatment as outlined below frequently will bring about relief and possibly cure.

The treatment in the past has been along one of these lines:

1. Medicinal or palliative
2. Neurectomy
3. Block anesthesia
4. Removal of the Gasserian ganglion or its sensory roots
5. Nutritional vitamin therapy

Medicinal Treatment.—It is always well to resort first to this treatment, for it will aid in verifying the diagnosis. It is well to remember that some patients suffer only intermittently in the beginning and this stage of intermittent mild attacks may last for months or even two or three years. Some local medicinal remedies have been employed in the treatment and have been eulogized unreservedly because of the cessation of pain following their application. No doubt in many cases this was merely a coincidence. Therapeutic and palliative drugs have been administered to allay the pain of this distressing malady. There is no specific drug treatment for the cure of tic douloureux. Some of the drugs which have been used with a variable degree of success are as follows: codeine, phosphorus, iron, trichlorethylene, arsenic, strychnine, quinine, pentobarbital sodium, aspirin and nitroglycerine.

Many patients suffering from tic douloureux have become habituated to morphine and opium. Physicians and dentists should be very careful in prescribing such drugs because of the possibility of the patient forming a drug habit. If a positive reaction to the Wassermann test is obtained and syphilis is diagnosed, then by all means a thorough treatment for syphilis must be given.

The wholesale extraction of teeth has been resorted to by some operators, only to find that in many cases after the teeth have been removed, the patient has sacrificed a good set of teeth with no relief. Therefore utmost care should be taken before resorting to forceps and making the patient a dental cripple.

Neurectomy.—Many ingenious methods of performing neurectomy are used in treatment of this condition. Some of these methods are of great value for relief and cure of patients with peripheral disturbances, who in many cases cannot undergo any serious surgical procedure. The nerve branches that are most commonly removed are the infra-orbital and supra-orbital, nasal and inferior dental, after which the foramen is plugged with ivory or some noncorrodible metal.

Block Anesthesia.—Two per cent procaine hydrochloride always is injected prior to alcoholization for two reasons. First, it aids in confirming the diagnosis of which branch is involved and, secondly, it makes the alcohol injection much less painful. It is known that alcohol injection in nerve tissue has a destructive action, and its comforting effect in the treatment of tic douloureux is a result of the degeneration of the nerve branches or ganglions. Deep injection of alcohol should be made under strictly aseptic conditions with the patient in a semi-supine or horizontal position. The alcoholization of any nerve or ganglion is a surgical

UMI

procedure which requires experience, judgment and knowledge of technic. The atrophic disturbance that may follow the blocking is proportional to the degree of nerve destruction; in the aged or feeble patients better results may be obtained by blocking with alcohol in preference to neurectomy or a section of a sensory root. The reaction produced by alcohol when injected in any kind of tissue is degenerative. The extent to which this is produced depends on the kind of tissue injected. For example, the skin and muscle tissues are not affected to such an extent as the loose connective or nerve tissue. In other words it produces the greatest destructive effect on highly organized tissue such as the ganglion, nerve trunk or brain tissue.

The pathologic process which takes place following an alcoholic injection is that of an aseptic necrosis, the necrotic tissue being replaced in time with fibrous connective tissue. Therefore it is very important to use every measure of aseptic technic while making a deep block injection, because if the necrotic tissue should become infected the outcome may be serious. If an alcoholic solution is injected beneath the skin, it produces a painful burning sensation and if injected in sufficient quantities may produce sloughing. The operator never should inject more alcohol than is absolutely necessary to produce the desired results. This amount averages 1 to 2 cc. of absolute alcohol, or 80 to 90 per cent aldehyde free alcohol.

Nutritional and Vitamin Approach.—The first application of this method for relief of symptoms of major trigeminal neuralgia or tic douloureux was performed by a group of research workers at the California Institute of Technology. This work was carried on by Borsook, Kremers and Wiggins in 1940.[1,2] Their report covers 58 cases observed over a period of fourteen months. All patients were given large doses of thiamin chloride hypodermically, in addition to a concentrated liver extract high in anti-pernicious anemia principle. All were observed for six to fourteen months with the result that 37 showed marked improvement, 15 moderate improvement, 3 slight improvement and 3 did not improve. Of the 52 patients that improved, 38 had remissions during and subsequent to the course of vitamin therapy, which lasted longer than any spontaneous remission during the two year period preceding the beginning of the treatment.

While treating some of these patients who had been started on the regime of Borsook, Kremers and Wiggins, it was felt by the author that perhaps the proper place for thiamin chloride is in the intestinal tract since it is excreted so quickly through the kidneys when administered parenterally. Also because niacinamide and nicotinic acid are peripheral arterial stimulants and ascorbic acid acts as an oxidizer of tissue cells, why could not these be combined with a high protein and a minimal refined carbohydrate diet?

This theory developed from the perusal of the history of 49 patients who were seen with various intensities of tic douloureux. These histories frequently indicated poor nutritional habits, in some instances because of psychic trauma such as a sudden death, divorce or a great loss of money, with the resulting impaired appetite. The total calories consumed by each patient dropped sometimes as low as 1,000 calories daily, consisting mainly of carbohydrates. Approximately 80 per cent of them partook very heavily of sweets which replenished energy but

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1. Borsook, H.; Kremers, M. Y., and Wiggins, C. G., The Relief of Symptoms of Major Trigeminal Neuralgia (Tic Douloureux). *J.A.M.A.* 114:1421 (April 13) 1940.
2. Borsook, H.; Kremers, M. Y., and Wiggins, C. G., The Relief of Symptoms in Major Trigeminal Neuralgia (Tic Douloureux) Following the Administration of Massive Doses of Vitamin B_1 Supplemented in Some Instances by Concentrated Liver Extract. Abstract of a report read at the National Academy of Sciences, Washington, D. C., April, 1939. *Science* 89:439 (May 12) 1939.

UMI

decreased normal appetite and brought about faulty nutrition. Very little red meat, proteins or dairy products were consumed. The majority of them had, in addition to a lack of appetite, developed the laxative habit. This led to the belief that susceptibility to tic douloureux could be related closely to the nutritional state and vitamin sufficiency of the body. Protein requirements in adulthood are admittedly less than in childhood but nevertheless are rather high and conceivably may be increased by excessive use of laxatives which impair protein and vitamin absorption and utilization. Chronic constipation which is induced by laxatives such as mineral oil may lead to a lower protein absorption from the bowel and its utilization in the body cells.

Older persons often develop a distaste for meat; therefore, in spite of lower metabolic requirements, great care should be exercised to make certain that the actual protein intake does not fall below an amount commensurate with health. Naturally, with this pain there is a further disturbance involved in the consumption of protein foods because they are not masticated as easily as are carbohydrates, which satisfy the necessary energy and heat requirements but fail to replenish the body with protein factors necessary to replace cell protoplasm. In infancy, childhood and early adulthood, tic douloureux is rare, and protein requirements are relatively much higher in relation to the body weight than for a normal adult of older age. This is clear when one considers that, normally, protein is retained for tissue synthesis and a stronger positive nitrogen balance must be maintained. Careful analysis of food consumed by most of these patients with major trigeminal neuralgia proves that it does not come up to minimal standards found necessary to maintain adequate supply of essential tissue-building nutritional factors.

Defective nutrition can arise when the diet seems adequate because of some disturbance in the state of the gastro-intestinal tract and its secretions which may act adversely so as to condition or enhance deficiency of nutritional factors within the body proper. Protein deficiency in itself may lead to actual edema of the intestinal mucosa resulting in poor intestinal absorption, thus completing a vicious cycle. Food and vitamins by way of the mouth is the most effective method for the administration of necessary nutritive factors.

Correction of achlorhydria and a daily diet of 2,000 calories, minimizing the carbohydrates, giving a protein consumption of 125 Gm., carbohydrate consumption of 250 Gm., and the administration of vitamins containing thiamin, riboflavin, nicotinic acid and ascorbic acid seem to do the work of relieving the patient of this difficulty. Because this is a preliminary report, statistical analysis of the data is not completed yet, but a survey of the data indicates that control of dietary factors alone has brought relief to many. The percentage of favorable results is near or a bit higher than that obtained in the studies at the California Institute of Technology, but more patience and much more time will reveal if we are on the right track. It is hoped that someone will find the chemical or drug that will cure rather than merely relieve these suffering people.—*65 North Madison Street.*

Comment

This preliminary report is of interest to oral surgeons. The failure of neurologists and neurosurgeons to establish a definite cause for major trigeminal neuralgia justifies any logical approach to the problems of treatment of this distressing condition. Improvement of general nutrition and the accompanying

improvement of the nutrition and state of nerve tissue is well worth clinical trial in every case. In the event major surgery becomes necessary, the patient will be in much better condition to undergo operation. In severe cases where alcohol injections usually afford relief for a period of six to nine months or more and accustom the patients to resulting anesthesia, nutritional therapy surely is indicated for it well might prevent or reduce the intensity of the pain that tends to recur after the recovery from the anesthesia from alcohol injection. In any event the patient's well being will be improved greatly, and surgery if indicated will be less hazardous. Further clinical research in this approach to the problem is indicated in numerous centers.—*Editor.*

GRADUATE COURSE IN ORAL SURGERY

A two year, full time graduate course in the basic sciences, with limited clinical experience, is being offered by the Department of Oral Surgery at the College of Dentistry, University of Illinois. Credit toward a Master of Science degree is being given. Applications are being accepted now for September, 1948.

Further information can be obtained from the Graduate Division, College of Dentistry, University of Illinois, 808 S. Wood Street, Chicago 12.

ATLAS OF DENTAL AND ORAL PATHOLOGY

The American Registry of Pathology recently has released the fourth edition of the *Atlas of Dental and Oral Pathology* which was prepared at the Army Institute of Pathology from material in the Registry of Dental and Oral Pathology of the American Dental Association.

In many respects this latest edition is a completely new publication. The text used in previous editions has been revised extensively by the authors, Lt. Col. Joseph L. Bernier and Col. James E. Ash. The illustrations have been replaced with more suitable ones, and presentation of the material has been rearranged. It now contains 230 pages and 484 illustrations.

Copies of the *Atlas,* which sells for $7, can be obtained from the Registry Office, Army Medical Museum, Washington 25, D. C.

RESEARCH SCHOLARSHIP

An annual scholarship of $1,000 for research in clinical oral pathology has been established by the New York Institute of Clinical Oral Pathology. Information can be obtained from the executive secretary of the Institute, G. Roistacher, 101 East 79th Street, New York 21.

UMI

THE USE OF PROTEIN IN ORAL AND MAXILLOFACIAL SURGERY

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Harrisburg, Pa.

DURING the past decade or so, there has been a striking improvement in the mortality and morbidity rate of surgical patients; this has been brought about by improvements in anesthesia and technical procedures. However, another reason has been better preoperative and postoperative care of patients. This has come about through orientation in the biological sciences in some of the educational programs. The application of the material derived from study and research in these subjects to clinical phenomena keeps surgery dynamic. It is not possible to consider all phases of importance in preoperative and postoperative care, so the following discussion will be limited to the use of protein. It is the purpose of this paper to review briefly some of the experimental evidence as a foundation and then attempt to show how patients being submitted to oral and maxillofacial care might be benefited from the clinical use of this material.

Nitrogen Balance

It is customary when speaking of protein to use the term nitrogen balance. This is because all protein contains 16 per cent nitrogen, and the loss of protein is determined by measuring the nitrogen of the urine and multiplying that figure by 6.25. Loss by other routes is fairly constant. A patient is said to be in nitrogen balance when the intake and the loss of protein are equal. When the intake is greater, it is referred to as a positive balance, and when the loss exceeds, a negative balance.

Loss of protein frequently is associated with starvation, ill-advised dieting, diseases of the liver and kidney, gastro-intestinal disturbances, hemorrhage, serum exudation, burns, operations, trauma, infections, febrile states, hypermetabolic states, ether anesthesia and in some less important situations. The effects of an inadequate protein intake begin immediately but are insidious and fairly well tolerated so that protein needs often are overlooked. An inadequate intake may be instituted in oral surgery patients with operation, infections, malignancies, sore mouth as in cases of post-irradiation therapy, tuberculosis, chronic aphthous stomatitis and others, intermaxillary fixation for fractures, bone grafts, osteotomies, ostectomies, the prolonged use of opiates, or the patient may be apprehensive about eating after any surgical procedure.

Effects of Protein Intake on Wound Healing

Experiments have shown that a protein deficiency retards, while a high protein intake accelerates, wound healing. In a review by Koster,[1,2] 86 per cent of patients with an infection or disruption of a wound after operation were found to have an average serum albumin of 3.75 mg. per 100 cc. which is at the lower

Read at a meeting of the Chalmers J. Lyons Academy of Oral Surgery at Ann Arbor, Mich., on January 28, 1948.

1. Koster, H., and Kasman, L.P., The Relation of Serum Protein to Well Healed and to Disrupt Wounds. *Arch. Surg.* 45:776 (November) 1942.
2. Koster, H., and Shapiro, A., Serum Proteins and Wound Healing. *Arch. Surg.* 41:723 (September) 1940.

UMI

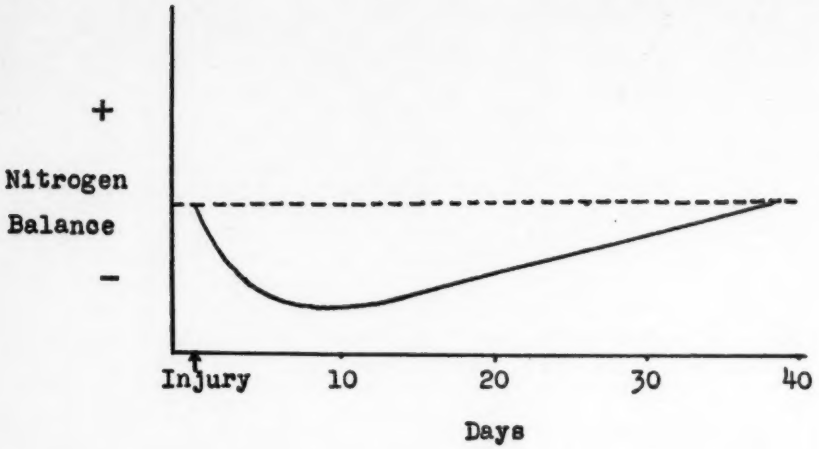

Fig. 1.—Traumatic loss of protein which occurs in some fractures

level of normal. Normal values are about 3.0 to 4.5 mg. per 100 cc. Only 20 per cent of the patients with a clean wound showed the same level. In other words, patients with infection, or those who developed infection and dehiscence of the wound, showed a lower level of serum albumin, or protein. Further, patients in a poor nutritional state, of which hypoproteinemia is a part, will favor infection and disruption of the wound.

Rat experimentation conducted by Localio and associates[3] has shown a slowed proliferative period, a lowered tensile strength and a delay in wound healing on a deficient protein intake. Lowered tensile strength is caused by diminution in the number of fibroblasts and a delay in the formation of mature collagen. Disturbed colloidal osmotic pressure is also an important factor. The wounds also demonstrated an increase in secretions and infections. Albumin is important in drawing tissue fluid back into the vascular system under colloidal pressure; hence, when the albumin level is low, fluid tends to accumulate in the tissues and at the wound site.

A reduction of 15 per cent of plasma protein is said to cause a moderate delay, and a reduction of 25 per cent a serious delay or complete failure of healing. Protein values are not always positive clues for they may be erroneously high in dehydration, or the globulin fraction may increase in the presence of infection while the more important albumin fraction is decreased. It is advisable to obtain the ratio of albumin to globulin as well as total protein. If a patient has received whole blood or plasma, the serum protein level may be normal with tissue protein yet depleted. It has not been decided whether the liver cells, tissue cells or both convert plasma protein to the specific form utilizable by the cells, but in any case time is involved. Protein is used first for hemoglobin, then plasma protein and lastly tissue protein. Ultimately a constant ratio of 1:30 is

3. Localio, S.A., Casale, W., and Hinton, J.W., Wound Healing—Experimental and Statistical Study: Experimental Observations. *Surg., Gynec. & Obst.* 77:243 (September) 1943.

established between plasma and tissue protein. When one part of plasma protein is lost, thirty parts of tissue protein are lost. There seems to be a dynamic equilibrium between the various protein stores, but again, it takes time to establish this equilibrium. A malnourished patient may be given a transfusion to build up the blood and plasma protein, then operated on only to die in the postoperative period for no apparent reason; this may be disintegration from lack of tissue protein. Food given by mouth is the most efficient method of supplying protein and is available more readily to the tissues than protein supplied by transfusion of blood or plasma.

The latent period in wound healing, which is the time from injury to tensile strength or fibroblastic proliferation and which usually is considered to be about four days, may be shortened almost to elimination by an adequate intake of protein according to Clark.[4] Harvey and Howes[5] feel the "lag period" is not decreased but that repair proceeds more rapidly on a high protein intake.

Loss of Protein with Trauma

Cuthbertson[6,7] of the University of Glasgow was the first in recent times to call attention to the negative nitrogen balance which commonly follows trauma. Howard[8,9] studied a group of fracture cases and found an average loss of nitrogen of 225 Gm. which is equal to 1,400 Gm. of protein or 15 pounds of muscle. The most intense loss of protein occurs between the fourth and eleventh days after injury; after this it diminishes, but it may be thirty to forty days before a positive balance is established. This has been referred to as a "toxic loss of protein" because it was felt to be due to liberation of a toxic substance at the wound site. "Traumatic loss of protein" seems to be more applicable, and the breakdown of tissue protein probably occurs to supply certain amino acids necessary for healing. Some rather simple fractures have shown this phenomenon. Therefore, it is the opinion of this author that patients, particularly those with multiple fractures of facial bones, show this phenomenon to a marked degree and not uncommonly lose many pounds in weight (Fig. 1).

Further, in these cases the intake is impaired. Operative cases show this reaction but to a lesser degree. The same can be applied to infections and burns. Experiments have shown that the loss of protein is from body tissues and not from the site of the injury except in the case of burns and massive infections where there are both local and general losses.

On the basis of the foregoing, it can be concluded, then, that protein is an essential adjuvant to the care of oral and maxillofacial surgical patients as well as in others. Treatment of the protein needs of these individuals depends largely on the dictates of the clinical picture and a knowledge of the development of such a deficiency. An acute loss of protein is tolerated poorly and occurs primarily in hemorrhage.

Few operations in oral surgery are associated with a significant blood loss, but most oral surgeons have, on occasions, seen prolonged bleeding following dental

4. Clark, A. H., The Effect of Diet on Healing of Wounds. *Bull. Johns Hopkins Hosp.* 30:117 (May) 1919.
5. Harvey, S.C., and Howes, E.L., Effect of High Protein Diet on Velocity of Growth of Fibroblasts in a Healing Wound. *Ann. Surg.* 91:641 (May) 1930.
6. Cuthbertson, D.P., Post-Shock Metabolic Response (Arris and Gale Lecture). *Lancet* 1:433 (April 11) 1942.
7. Cuthbertson, D.P., Further Observations on the Disturbance of the Metabolism Caused by Injury, with Particular Reference to the Dietary Requirements of Fracture Cases. *Brit. J. Surg.* 23:505 (January) 1936.
8. Howard, J. E.; Parson, W.; Stein, K.E.; Oisenberg, H., and Reidt, V., Studies on Fracture Convalescence: I. Nitrogen Metabolism After Fracture and Skeletal Operations on Healthy Males. *Bull. Johns Hopkins Hosp.* 75:156 (September) 1944.
9. Howard, J. E., Protein Metabolism During Convalescence After Trauma. *Arch. Surg.* 50:166 (March) 1945.

UMI

extractions to approach a state of shock. And shock is a frequent complication of severe maxillofacial injuries. The treatment in trauma of this type consists of whole blood transfusions; but plasma, which is of second choice, is more readily available and should be utilized while the patient is being typed and cross-matched to receive whole blood. The amount to be given depends on the patient's progress, but in such cases it should be at least 500 to 1,000 cc.

Chronic Protein Deficiency

Chronic protein deficiency should be suspected in disease situations already mentioned and should be assumed when the patient's loss of weight can not be explained by loss of water. Elective operations should be postponed temporarily to permit a good preoperative regimen, part of which will consist of a high protein intake. It usually takes at least one week to prepare a malnourished patient for operation. An intelligent clinical evaluation is the criterion in determining whether more time is needed. A rigid preoperative course of protein, as well as vitamins and other adjuvants not to be discussed in this paper, probably would eliminate some of the failures in grafts of bone and skin, ostectomies, palatorrhaphies and other procedures.

Needs of Patients with Fractures

The care of patients with fractures varies depending on the severity of the case with which nourishment can be taken. Whole blood and plasma will be needed in severe injuries. These patients also will demonstrate a traumatic loss of protein, so a high intake should be instituted early. After recovery from the initial effects of the injury, the intake by mouth probably will be inadequate for a few days. In general, the more severe the injury, the greater the need for protein and the less the patient's inclination to take adequate nourishment. The problem may be handled during this period in several ways. One of the many protein hydrolysate preparations now available can be given orally or parenterally or both depending on the specifications of the product. The intravenous forms usually contain 50 to 60 Gm. of mixed amino acids per liter, and so it becomes evident that at least two liters daily are necessary if no food is taken by mouth. The coefficient of utilization varies with different patients and different disease situations but is never 100 per cent.

Intravenous hydrolysates must be given slowly to insure a greater utilization and to reduce the incidence of reactions, thereby confining the patient to bed for long periods. One liter should be given at a rate requiring five hours or longer. Too rapid administration may result in symptoms of hyperamino-acidemia with nausea and vomiting, headache and flushing. If breakdown products of protein other than amino acids are present, a foreign protein reaction may be manifested. Thrombophlebitis has been a common complication.

Some of the hydrolysates have a very disagreeable odor and taste while some of the newer ones designed for oral administration are bland and tasteless. The latter can be given in plain or flavored milk, juices, broths, custards, puddings, meat loafs and so forth. Regardless of the route of administration, hydrolysates must be given with 1,500 to 2,000 calories of other foodstuff to meet caloric needs of the body and to spare amino acids for protein synthesis. To accomplish this by the intravenous route and still give 2 liters of a hydrolysate daily is impossible.

The problem is to give the patient 80 Gm. of protein daily and an additional

amount to take care of the loss. The sick or recently injured patient frequently cannot be persuaded to eat a natural diet containing 80 or more Gm. of protein because of the bulk of the usual protein foods and their high satiety value along with a decrease in appetite. The hydrolysates can be used to supplement the diet.

Methods of Feeding

Drip feeding by tube is a better way to supply protein early before the patient starts to eat. A Levine tube is passed through the nose into the stomach and left in place rather than to re-insert it several times a day. If vomiting is feared, the Wangensteen suction apparatus can be included in the setup. For such a feeding, a slight modification of one of the jejunostomy formulas available in hospitals is suggested.

Modified Formula for Drip Feeding by Tube

Powdered skim milk	600 Gm.
20 per cent cream	240 Gm.
Water	1,660 Gm.
Vitamins	
Total volume	2,500 cc.

These are high protein mixtures to which should be added more than the usual amount of water to give the patient an adequate fluid intake. One example of such a preparation yields 220 Gm. of protein, 54 Gm. of fat and 320 Gm. of carbohydrate with a total of 2,650 calories. It consists of 600 Gm. of powdered skim milk, 240 Gm. of 20 per cent cream and 1,660 cc. of water so that the mixture totals 2,500 cc. In some cases it will be advisable to add more water to bring the total volume to 3,000 cc. The cream is added to the water, the powdered milk is added slowly with constant stirring and finally strained to eliminate any lumps. To this formula should be added 500 mg. of ascorbic acid, 3 mg. of thiamin and 50 mg. of niacin. It is best to give this by slow drip throughout the night and intermittently during the day to permit the patient to be ambulatory if possible.

There are disadvantages to this program. Many patients do not tolerate the tube well for several days, but in most cases it will be necessary to use it only for a day or two. If the nose is fractured, it may be difficult to pass the tube; and also these rich mixtures often incite diarrhea. This will be less common when introduced into the stomach in a more dilute form than when used as a jejunostomy feeding.

As soon as the patient is taking adequate food by mouth, which is the natural and desirable way to feed all patients, a high protein, high carbohydrate, high vitamin, liquid diet of about 3,000 calories with supplements of ferrous gluconate and vitamins is recommended. Such a diet is usually low in thiamin, nicotinamide and iron, but it is easier to prescribe one of the multivitamin preparations. By reducing the fat, it is possible to increase the protein. Many feel that a high fat content is detrimental, but there is a tendency on the part of some workers at present to add more fat. A high protein diet in a hospital usually contains about 120 Gm. of protein, but there is evidence that a higher intake is advisable during the first two weeks after the injury. Interval feedings then become necessary and should consist of milk, eggnog or preferably a modified Varco[10] or similar formula, plain or flavored.

10. Varco, R. L. Preoperative Dietary Management for Surgical Patients, with Special Reference to Lesions of the Stomach and Duodenum. *Surgery* 19:303 (March) 1946.

UMI

Modified Varco Formula for Interval Feeding

Eggs	8
Skim milk	1,000 cc.
Skim milk powder	4 ounces
Lactose	300 Gm.
Salt and flavoring may be added.	
Total volume	1,500 cc.

Concentrated formulas like Varco's make it possible for a patient to be well nourished and at the same time keep the quantity of food relatively small. A slightly modified Varco's formula will supply 120 Gm. of protein, 37 Gm. of fat and 409 Gm. of carbohydrate with a total of 2,446 calories in a volume of 1,500 cc. It contains 8 eggs, 1,000 cc. of skim milk, 4 ounces of skim milk powder and 300 Gm. of lactose. Salt and flavoring may be added. This in itself satisfies the daily caloric requirements of most patients, but another 1,000 to 1,500 cc. of fluid are needed daily. Fruit juices should make up part of this deficit. This regimen then is deficient in iron, nicotinamide and thiamin. Appetite exerts a considerable influence on the quantity of nourishment taken, so it may be necessary to urge the patient to eat as well as to make food pleasing.

The 3,000 calorie diet just suggested is also the best pre-anesthetic and post-operative one although it need not be in the liquid form. It is known that the liver is damaged by some anesthetics and narcotics such as ether, alcohol, paraldehyde, chloral and others. Liver necrosis or damage is proportional to its fat content in part. Further, fat depresses respiratory enzyme systems and prolongs wound healing. Carbohydrate protects the liver only in so far as it replaces the fat content, it can be utilized by injured liver cells and it saves protein for anabolic processes. The probability of liver injury decreases as its protein content increases, and a fatty liver is less likely to be damaged if the protein content is high.

Protein favors respiration of cells and aids wound healing. It would seem then that a normal intake of fat would cause no harm as long as the protein and carbohydrate needs are satisfied. The best diet is the well balanced one which nature intended us to eat except in conditions where an increased intake of a foodstuff is evident.

With moderately severe injuries in which shock is not a factor and food can be started by mouth early, a 120 Gm. protein liquid diet with interval feedings of a concentrated protein mixture to assure an intake of over 120 Gm. of protein daily for two weeks would seem desirable. Whereas, with minor fractures a protein intake of 80 Gm. is probably adequate because the traumatic loss is of little consequence.

A liquid formula containing 80 Gm. of protein and 2,880 calories in a volume of 2,000 cc. can be prepared by mixing 1 pint of 20 per cent cream, 1 quart of milk, 5 eggs and 10 tablespoons of Karo syrup. This formula is deficient in ascorbic acid, thiamin, nicotinamide, and iron on the basis of the recommended allowance of the National Research Council. It also falls 500 to 1,000 cc. short in supplying an adequate daily fluid intake, so fruit juices can be given separately to supply ascorbic acid and make up part of the fluid deficit. The other vitamins should be replaced, and with intermaxillary fixation it is accomplished most easily with one of the liquid multivitamin preparations. Again, iron should be included if this program is to be followed any length of time. Dextrimaltose

can be substituted for the syrup and salt and flavoring may be added. It is best not to use a single formula as a source of food because of monotony, but the preparation just suggested also can be used for interval feeding.

Diet in Minor Surgical Procedure

Patients with a decreased food intake because of minor oral surgery procedures or a sore mouth caused by disease should do well on an 80 Gm. protein diet unless the deficiency is prolonged and associated with weight loss in which case the protein should be increased. Those with advanced cancer of the mouth are good examples of patients who need a higher protein intake.

Many patients who have multiple extractions start out on a dietary program that is inadequate. Some think only in terms of soups which are deficient and filling; one cup of broth, for example, contains 1 Gm. of protein or less. Others feel it is an opportune time to follow a diet and lose weight, but the evidence shows it is unwise to reduce the quantity of any foodstuff other than fats. With hospital patients, it is only necessary to order the appropriate diet and ask the

Include daily:

Milk, whole ..... 1½ quarts

Cream (40%) ..... 1 cup

Cereal ..... ½ cup (to be used as cereal gruel)

Cornmeal, strained	Oatmeal, strained
Farina	Whole wheat cereal, strained

Eggs 3

Vegetable, pureed ..... ½ cup (to be used in cream soups)

Tomato or tomato juice	Asparagus
Beans, green	Peas
Carrots	Potato
Corn	Beets

Fruits (juice of any fruit) ..... 4 cups

Orange	Peach	Apricot
Grapefruit	Pear	Blackberries
Pineapple	Grape juice	Apple juice

Sugar ..... 8 tablespoons
(honey, syrup can be used in place of sugar)

Butter ..... 1 tablespoon

Beverage (clear coffee, tea)

Seasoning (any)

(Powdered milk used to increase protein)

Fig. 2.—Summary of a 3,000 calorie liquid diet which can be distributed to patients (courtesy of dietetics department of the University Hospital, University of Michigan). The diet provides approximately 80 Gm. of protein, 3,000 to 3,200 calories per day. It is low in iron, thiamin and nicotinamide as compared to National Research Council allowances

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No. 1

Breakfast

Grapefruit juice—1 cup
Sugar—2 tsp.
Farina gruel—1 cup
Sugar—2 tsp.
Cocoa—2 cups
Sugar—4 tsp.

10:00 a.m.

Milk shake
Sugar—2 tsp.

Lunch

Cream of potato soup—1 cup
Mixed fruit juice—1 cup
Sugar—2 tsp.
Vanilla eggnog—1 cup
Sugar—2 tsp.
Beverage—1 tsp. sugar

3:00 p.m.

Milk and cream—1 cup

Dinner

Bouillon
Grape juice—1 cup
Sugar—2 tsp.
Soft custard—1 cup
Beverage—1 tsp. sugar

7:00 p.m.

Peach nectar with sugar—2 tsp.

No. 2

Breakfast

Apricot nectar—1 cup
Strained cornmeal gruel—1 cup
Sugar—2 tsp.
Chocolate milk—1½ cups
Beverage

10:00 a.m.

Milk and cream—1 cup

Lunch

Cream of pea soup—1 cup
Maple custard—1 cup
Large prune juice w. lemon—1 cup
Butter in soup—1½ pats
Beverage

3:00 p.m.

Vanilla milk shake—1 cup w. 1 egg

Dinner

Bouillon
Grapefruit juice—1 cup
Sugar—2 tsp.
Vanilla eggnog—1 cup
Butter in soup—1½ pats
Beverage

7:00 p.m.

Grape juice—1 cup

No. 3

Breakfast

Grape juice—1 cup
Sugar—2 tsp.
Farina gruel—1 cup
Sugar—2 tsp.
Whole milk—1 cup
Beverage

10:00 a.m.

Cocoa with 1 egg
Sugar—2 tsp.

Lunch

Cream of green bean soup—1 cup
Mixed fruit juice—1 cup
Sugar—2 tsp.
Honey eggnog—1 cup
Sugar—2 tsp.
Butter—1½ pats

3:00 p.m.

Tomato juice

Dinner

Cream of corn soup—1 cup
Peach nectar—1 cup
Sugar—2 tsp.
Vanilla custard—1 cup
Butter—1½ pats

7:00 p.m.

Pineapple juice—1 cup
Sugar—2 tsp.

UMI

No. 4

Breakfast	*Lunch*	*Dinner*
Pineapple juice—1 cup	Bouillon—1 cup	Cream of carrot soup—1 cup
Sugar—2 tsp.	Butter—1½ pats	Butter—1½ pats
Strained oatmeal gruel—1 cup	Apple juice—1 cup	Grapefruit juice—1 cup
Sugar—2 tsp.	Sugar—2 tsp.	Sugar—2 tsp.
Cocoa—2 cups	Lemon custard—1 cup, with cream—¼ cup	Maple eggnog (¼ cup cream) —1 cup
Sugar—4 tsp.	Sugar—4 tsp.	Sugar—2 tsp.
Beverage	Beverage	Beverage
	Sugar—1 tsp.	Sugar—1 tsp.
10:00 a.m.	*3:00 p.m.*	*7:00 p.m.*
Chocolate malted milk—1 cup with 1 egg	Milk and cream—1 cup	Grape juice—1 cup
Sugar—2 tsp.	(½ cup each)	Sugar—2 tsp.

No. 5

Breakfast	*Lunch*	*Dinner*
Mixed fruit juice—1 cup	Cream of pea soup—1 cup	Cream of tomato soup
Sugar—2 tsp.	Apricot nectar—1 cup	Pear juice—1 cup
Wheat cereal gruel—1 cup	Sugar—2 tsp.	Sugar—2 tsp.
Sugar—2 tsp.	Chocolate custard (¼ cup cream) —1 cup	Vanilla pudding (¼ cup cream) —1 cup
Milk—whole, 2 cups	Sugar—4 tsp.	Sugar—4 tsp.
Beverage		Beverage
		Sugar—1 tsp.
10:00 a.m.	*3:00 p.m.*	*7:00 p.m.*
Apple juice—1 cup	Strawberry milk shake	Lemonade—1 cup
Sugar—2 tsp.	(with 1 egg and 2 tsp. sugar—1 cup)	Sugar—2 tsp.

Fig. 3.—A suggested menu for the 3,000 calorie liquid diet (courtesy of the dietetics department of the University Hospital, University of Michigan)

dietitian to instruct the patient before discharge. But in a busy office practice there is not enough time to discuss diet with the patients and they are apt to forget much of what has been said.

A dietitian should be consulted to set up a soft and a liquid diet of 2,000, 2,500, 3,000 and 3,500 calories containing both 80 and 120 Gm. of protein. These, together with instructions for preparing concentrated protein formulas, can be mimeographed and distributed to patients who need such information. The 80 Gm. protein diet of 2,500 and 3,000 calories for females and males, respectively, will be the most popular in the office. The elderly lady who sits at home most of the time will need 2,000 calories or less. The average student or office worker needs about 3,000 calories, while the heavy laborer needs up to 4,500 calories a day. Merely decide on the patient's needs and prescribe the appropriate program, one type of which is illustrated (Figs. 2 and 3). It is true that many patients will not follow the program rigidly, but most individuals will be surprised when their attention is called to the number of foods they can eat. Many will have operative procedures which will not interfere with food consumption, but some should have instructions.

Summary and Conclusions

In summary, then, it is evident that protein is an important nutritive tool in the treatment of oral and maxillofacial surgery patients as well as in others. Severe maxillofacial injuries will require whole blood and plasma followed by a high protein intake for two weeks after which it may be reduced gradually to a normal intake in four to six weeks. Moderately severe injuries also will require additional protein early, while minor injuries should do well as long as a standard intake of 80 Gm. of protein is maintained.

Some operative cases and chronic disease situations will need added protein to benefit the patient. Those being subjected to minor surgical procedures need only instructions on a standard intake. In the case of major elective operations, the patient should be given the benefit of an adequate preoperative regimen. A patient's needs usually can be determined best by an intelligent clinical evaluation with laboratory examinations being considered as substantiating evidence. The best diet is the well balanced one composed of natural foodstuffs and fed into the gastro-intestinal tract. But at times an additional amount of one foodstuff is needed.—*813 North Second Street.*

AMERICAN BOARD OF ORAL SURGERY

Examinations for certification by the American Board of Oral Surgery will be held in Chicago on September 7 and 8, 1948.

Requests for application forms or additional information should be addressed to Leslie M. FitzGerald, secretary, 718 Roshek Building, Dubuque, Iowa.

EOSINOPHILIC GRANULOMA OF BONE WITH REPORT OF CASE

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THE EXISTENCE of eosinophilic granuloma of bone occurs more frequently than was supposed formerly; or, at least, our ability to recognize this disease has improved appreciably. There is a great deal of confusion and disagreement in the literature concerning the so-called xanthomatoses and the relation to the latter of Schuller-Christian's disease, Letterer-Siwe's disease, eosinophilic granuloma and certain other conditions that are regarded as "essential xanthomatoses." This group of diseases is of particular importance to the dentist because of oral lesions that simulate other more common ulcerative processes. Inability to establish a proper differential diagnosis and the use of purely local treatment in some of these conditions easily may lead to dire consequences in so far as the prognosis of the patient is concerned.

Therefore, a brief history of the evolution of these morbid processes will be outlined along with their differential diagnoses from a clinico-anatomic viewpoint. Considerations of etiology, treatment and prognosis will be discussed briefly. Further, a presentation will be made of a case of eosinophilic granuloma of bone that came to the attention of the author at the University of California Hospital.

Clinico-Anatomic Concepts

Eosinophilic granuloma of bone is stated to be an acute manifestation of a basic disease process in a class with chronic variants such as nonlipoid histiocytosis (Letterer-Siwe's disease) and lipogranulomatosis (Schuller-Christian's[1,2] disease).[3] Farber[4] is in agreement with this thesis. He states that "there is no indication that any of these conditions is a xanthomatous process or a primary alteration of lipid metabolism." Lichtenstein[4] in an article published in 1940 (quoted by Farber) considered eosinophilic granuloma as a separate disease entity from Schuller-Christian's disease. In a later article,[5] however, he agrees that Letterer-Siwe's disease, Schuller-Christian's disease and eosinophilic granuloma of bone "constitute different clinical expressions of the same basic disorder, which seems to predilect the hemopoietic system."

Letterer-Siwe's Disease (Reticulosis or Nonlipoid Histiocytosis).—This disorder may occur in infancy or early childhood, frequently in a rapidly fatal form in which histiocytic lesions are distributed widely through the soft tissues (especially lymphoid tissue) and the skeleton. It usually occurs in infants or children below the age of 2. It rarely appears after the age of 4. It usually runs an acute or subacute course, fatal within a matter of weeks or months.

1. Thannhauser, S. J., Xanthomatosis. In *Oxford Medicine*, edited by H. A. Christian. New York: Oxford University Press, 1940, vol. 4, chap. 7A, pt. 3, p. 214.
2. Kennedy, R. L. J., Xanthomatosis: Schuller-Christian's Disease. *Proc. Staff Meet., Mayo Clin.* 13:776 (December 7) 1938.
3. Shafiroff, B. G. P., and Scheman, L., Solitary Eosinophilic Granuloma of Rib; Case Report. *Ann Surg.* 125:510 (April) 1947.
4. Farber, Sidney, The Nature of "Solitary or Eosinophilic Granuloma" of Bone. *Am. J. Path.* 17:625 (July) 1941.
5. Jaffe, H. L., and Lichtenstein, Louis, Eosinophilic Granuloma of Bone. *Arch. Path.* 37:99 (February) 1944.

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The principal clinical findings are: a febrile course, enlargement of the spleen, liver and superficial lymph nodes; a cutaneous eruption, often purpuric in character; hypochromic secondary anemia, often profound, terminally, and one or more destructive lesions in bones, especially in the skull bones.[5] Other morbid manifestations also may appear, but the above are the most significant findings.

Histo-anatomically, Letterer-Siwe's disease is characterized by a wide dispersion of histiocytes through the tissues of the body. Nodular foci of these cells commonly are found. A histo-anatomic relation can be seen between Letterer-Siwe's disease and eosinophilic granuloma of bone; thus "the granulation tissue present in the destructive skeletal lesions of Letterer-Siwe's disease in an early stage of their evolution may be indistinguishable, microscopically, from such tissue in corresponding lesions of eosinophilic granuloma of bone."[5] It is interesting to note that only in destructive lesions of bones (early in their evolution) does one find large numbers of eosinophils coloring the histiocytic granulation tissue. The lesions in internal organs and lymph nodes in Letterer-Siwe's disease fail to show this imprint of eosinophils. Conversely, in older, more chronic skeletal lesions which have run for a year or more (in Letterer-Siwe's disease) considerable fibrous scarring of the inflammatory tissue and the transformation of some of the many histiocytes into "lipophagic foam cells"[5] are seen. This may be indistinguishable from the lipogranulomatosis that is supposedly characteristic of Schuller-Christian's disease. Glanzmann[6] maintains that Letterer-Siwe's disease may pass over into Schuller-Christian's disease. He regards the pathologic process as being represented in the acute, septic form by Letterer-Siwe's disease and in the more chronic form by Schuller-Christian's disease.

Schuller-Christian's Disease (Lipogranulomatosis).—It formerly was believed that the Christian triad,[7] diabetes insipidus, exophthalmos and calvarial defects, had to be present to establish a diagnosis of Schuller-Christian's disease. It has been shown now that this is not true. The presence of the Christian triad is dependent entirely on extensive involvement of the skull bones. It is not essential for diagnosis or specific for the disease. The prognosis of this disease is serious if, because of lesions of the skull, the hypothalamus, infundibulum or pituitary gland have been injured. Lesions of the lungs may scarify and cause failure of the right heart.

Histo-Anatomy.—Any case placed in the category of this disease should be expected to show, anatomically, collagenized and lipidized lesions classifiable as lipogranuloma. It must be pointed out, however, that "the fibroblastic scarring and collagenization and the varying amounts of cholesterol (free or in the cytoplasm of lipophagic foam cells) which give the characteristic lipogranuloma imprint to the lesions of Schuller-Christian's disease represent secondary engraftments on an inflammatory lesion originally neither scarred or lipidized."[5] In the opinion of Lichtenstein and Jaffe,[5] a case should not be designated as one of Schuller-Christian's disease unless or until the lesions possess some of the cytologic characteristics of lipogranuloma.

Eosinophilic Granuloma of Bone.—This "basic disorder" may occur in children or young adults in a relatively benign and much more localized form wherein lesions appear to form only in the skeleton (often in a single bone).[8] These lesions readily heal after simple curettage even without supplementary

6. Glanzmann, E., Infektiose Retikuloendotheliose (Abt-Letterer-Siwe'sche Krankheit) und ihre Beziehungen zum Morbus Schuller-Christian. *Ann. Paediat.* 155:1 (April) 1940.
7. Rowland, R. S., Pediatric Investigation of Essential Xanthomatosis, Schuller-Christian Type. *Tr. Am. Pediat. Soc.* 44:73, 1932.

roentgenotherapy. They even may resolve without interference by therapeutic measures.

The etiology is unknown.[8] Otani and Ehrlich[9] have stated that trauma may be an initiating factor.

Clinical Symptoms.—Pain and swelling are the most common complaints.[8]

Roentgenographic Findings.—According to Green and Farber,[8] the lesions vary in contour, being round, oval or irregular in outline. They present a "punched out" effect without cortical expansions. Where multiple lesions were present the picture represented that seen in metastatic malignancy or multiple myeloma, and it was identical with that seen in Schuller-Christian's disease. Flat and irregular bones were effected most commonly.

Treatment.—Radium and roentgen rays probably provide the most valuable treatment.[10]. Jaffe and Lichtenstein[5] recommend curettage with or without supplementary roentgenotherapy.

The prognosis is generally considered good.

Histo-Anatomy.—A skeletal lesion of only a week or month's duration (and not modified by a fracture through it) appears grossly as a more or less hemorrhagic and cystic area from which only a relatively small amount of granulation tissue can be curretted. If not necrotic this tissue is found histologically to consist essentially of histiocytes, including some "revealing phagocytic activity" interspersed among which are more or less prominent accumulations of eosinophils—especially eosinophilic leukocytes.[5] Thus there is very little, if any, scarring. However, if a fracture through the site of the lesion has been followed by a reparative reaction to it, considerable scarring may be present. Even in such a scarred lesion one may see, histologically, the typical picture of granulation tissue dominated by histiocytes which are intermingled with eosinophils. The presence or absence of scarring of the lesion associated with fracture does not represent necessarily a phase in the natural healing of eosinophilic granuloma. Lichtenstein and Jaffe[11] believe the untreated lesion will heal through resolution.

Thus these three conditions constitute "related expressions of the same basic disorder." Their lesions are characterized at the start by the presence of large numbers of histiocytes. The basic anatomic disorder thus appears to be a "peculiar inflammatory histiocytosis."[5]

The case described in this paper was referred to the dental surgery from the medical clinic. The dental findings were so unusual that it was decided to follow the case through. The actual medical, surgical, and laboratory work reported here, except for the dental examination and the review of the literature, was done in the University of California Hospital and Medical School. It is presented here because of peculiar mouth symptoms found and the difficulty encountered in diagnosing the condition.

Report of Case

The patient was a boy, aged 3 years and 9 months. Nine months previously his mother noted that he had a very fetid breath, although he was apparently in good health. A physician had treated him for a "sore throat." About a month later his mother noticed a swelling of the gin-

8 Green, W. T., and Farber, S., "Eosinophilic or Solitary Granuloma" of Bone. *J. Bone & Joint Surg.* 24:499 (July) 1942.

9. Otani, Sadao, and Ehrlich, J. C., Solitary Granuloma of Bone Simulating Primary Neoplasm. *Am. J. Path.* 16:479 (July) 1940.

10. Austin, L. T., Xanthomatosis (Schuller-Christian's Disease): Report of Dental Findings in One Case. *J. Oral Surg.* 4:209 (July) 1946.

11. Lichtenstein, Louis, and Jaffe, H. L., Eosinophilic Granuloma of Bone, with Report of Case. *Am. J. Path.* 16:595 (September) 1940.

givae on the upper left buccal surface. Her description of the left lower gum was that it was "black, eaten away and had pus on it." This gradually spread to the lower anterior teeth. About two months previously the left lower anterior and posterior deciduous teeth were removed as they were exfoliating. About three weeks before presentation, the gingivae of the left mandible became inflamed."

Treatment up to the time of entry in the hospital consisted of two days' administration of penicillin about two months previously. A mouthwash and some "powders for the mouth" also were given.

The patient had lost from 5 to 8 pounds in the last eight months. An increase in fatigability and anorexia had occurred. There had been no fever, cough nor gastro-intestinal upsets.

The jaw had been lanced along the inferior border of the body of the left mandible, about two months prior to the admission, with definite relief of swelling in the jaw. There was no history of tuberculosis, diabetes, tumors, blood dyscrasias or allergies.

There had been a tender swelling around the right ear for two weeks. The eyes had been red and droopy recently; they had a tired and dull appearance.

There had been no nausea, vomiting, diarrhea or abdominal pain.

Clinical Observations.—The patient was a fairly well developed and well nourished boy. He walked about and apparently was in no distress. There were a few cervical and axillary lymph nodes palpable.

The left maxillary buccal plate was resorbed up to the tips of the apices of the deciduous molars; the soft tissue was highly inflamed. Hard, gray "plaques" that could be flicked off were encrusted around the teeth and soft tissues.

In the left mandible the first permanent molar already had erupted. The tissue around it was very necrotic, similar to severe Vincent's infection. The left mandibular deciduous teeth had been extracted, since they had been exfoliating. There was a grayish, soft, purulent looking exudate along the soft tissue on the upper surface of the body of the left mandible. This could be removed only with difficulty and returned again in a matter of hours. One or two regions of

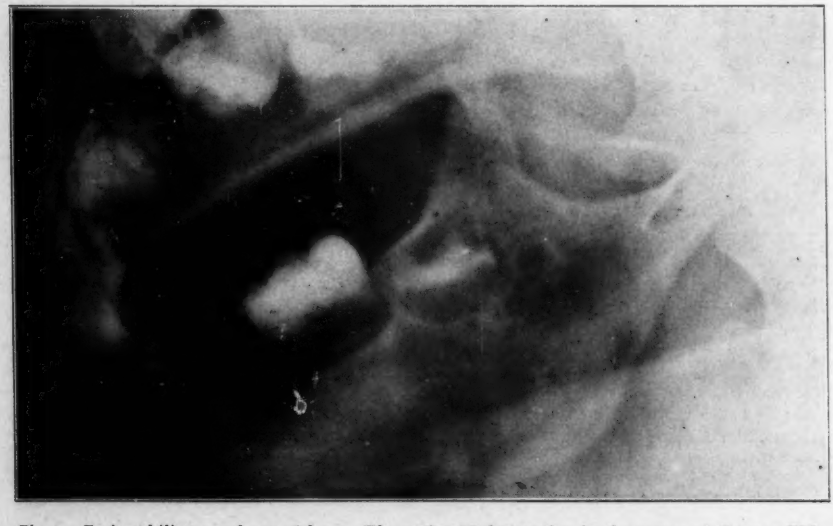

Fig. 1.—Eosinophilic granuloma of bone. The region of destruction in the ramus of the mandible can be seen clearly. The exfoliating first permanent molar and rarefaction of the body of the left mandible should be noted

denuded bone could be observed on the body of the mandible. These regions all were very sensitive to any attempted instrumentation.

There was a slight swelling of the left jaw, and an old scar from a fistulous tract was discernible on the skin over the lateral side of the left mandible.

The throat appeared to be free from infection.

Adenoids were present in the nasopharynx; the patient was a mouth breather. The oropharynx was free from infection.

The heart and lungs were normal.

Roentgenographic Examination.—Tangential films taken of the right skull showed a 1 by 2 cm. "punched out" region of rarefaction just anterior and below the point of junction of the lambdoid and squamosal sutures in the right temporal bone. No other destructive lesions were seen in the skull.

A definite oval region of bone destruction was visible in the left mandible near the ramus (Fig. 1). The deciduous teeth had been shed prematurely and the remaining molar tooth on the affected side was erupted far ahead of schedule.

Laboratory Observations.—The blood count showed: hemoglobin 12.5 Gm. per 100 cc. (average for several days); erythrocytes 4,700,000 per cubic millimeter; leukocytes 16,000 per cubic millimeter; the differential count was normal; the erythrocytes were normochromic and normocytic; the platelets were normal. In one early count 6 per cent myelocytes were found. Myelogenous leukemia was considered at the time.

Chemical analysis of the blood revealed cholesterol to the 160 mg. per 100 cc. of whole blood; serum albumin 4.22 Gm. per 100 cc.; serum globulin 4.15 Gm. per 100 cc.; serum calcium 10.9 mg. per 100 cc.; serum phosphorus 5.0 mg. per 100 cc.; basic phosphatase 11 Bodansky units, and ascorbic acid level 0.5 mg. per 100 cc.

The urine was normal.

The capillary fragility test produced 1 petechia in one minute at 20 mm. Hg. suction.

In the bacteriologic examination a smear of mandibular plaque material contained streptococci and was negative for spirochetes and fusiform bacilli. A bacteriologic culture of the same material showed Streptococcus viridans to be present and was negative for beta hemolytic streptococci.

Result of the coccidioidin test were negative, as were those of the tuberculin and Schick tests.

Biopsy.—A biopsy was taken on September 5, 1947, from material curetted from the skull lesion at the University of California Hospital.

Grossly, the specimen consisted of (1) about seventy-five small fragments of bone, each measuring roughly 0.2 to 0.3 cm. in size, and were irregular in size and shape; (2) a small, ovoid mass of pink tissue measuring 1 by 1 by 1.5 cm. in size, with several small, white flecks noted on the cut surfaces, and (3) a flattened piece of pink tissue, granular in appearance, soft in consistency, measuring 0.2 by 1.5 by 2 cm. in size.

In the histopathologic examinations (1) sections of bone showed dense trabeculae adjacent to which, in one region, was seen an accumulation of large cells with one or two ovoid, vesicular nuclei and homogeneous, eosinophilic cytoplasm. One or two giant cells were seen. In an adjacent region connective tissue showing fibroblastic hyperplasia was seen. (2) Sections of this tissue (Fig. 2) showed masses of cells with rounded or oval, vesicular nuclei with fine, granular chromatin and small nucleoli. These cells had a moderate amount of eosinophilic cytoplasm which appeared vacuolated. Numerous eosinophilic leukocytes were seen, and many engorged capillaries were present. A scattering of polymorphonuclear leukocytes and lymphocytes were seen throughout the section, and a few giant cells were noted. (3) Sections showed dense, collagenous fibers which in some regions were hyalinized. Strands and masses of the larger cells just described in (2) were seen. Giant cells were present, and eosinophils were numerous.

Diagnosis.—Eosinophilic granuloma of bone.

Treatment.—Roentgenotherapy and surgical curettage were used. The prognosis was favorable.

Follow-up.—On October 20, 1947, the patient was re-examined. He apparently had been well since his discharge about a month previously. He had complained of pain of his mouth on one occasion only. No more teeth had fallen out. His breath was still fetid but somewhat improved.

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The previously described defect in the right temporal bone was about 3 cm. in diameter. This was presumably a surgical defect superimposed on the pre-existing lesion. The lesion in the left mandible appeared slightly larger than before. There was a round region of decreased density approximately 1 cm. posterior to the previously described lesion. This measured about 0.5 cm. in diameter.

Conclusion.—The defect in the right temporal bone, 3 cm. in diameter, was caused by surgery.

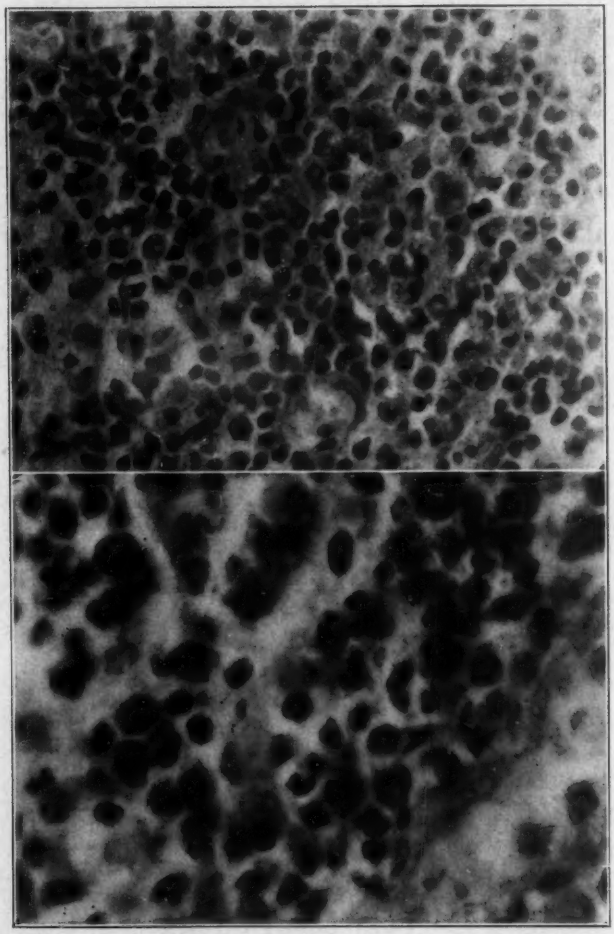

Fig. 2.—Eosinophilic granuloma of bone. These photomicrographs, taken from the biopsy section of the skull lesion, illustrate the granulomatous nature of the disease process. The large numbers of eosinophilic leukocytes are characteristic of the disease. A considerable number of large mononuclear cells and lymphocytes are also present. Above: x 110. Below: x 600

There was an increase in the extent of the lesion of the left mandible. There was no other clinical evidence of progression of the disease.

On March 22, 1948, he had improved but had lost his upper left deciduous second molar tooth, the roots of which were bared at the time of the last examination. There was no evidence of advancement of the disease. Roentgenograms of the skull and mandible showed the previously described defect in the right temporal bone, but it was defined less distinctly than before. The lesion in the superior border of the left mandible appeared to have decreased somewhat in size and the margins were slightly more dense than before. No new lesions were demonstrated.

On April 19, 1948, there was no apparent change. Roentgenograms showed no new lesions, and there was a filling in of the previously noted radiolucent regions. The last roentgenotherapy on both the left mandible and the right posterior auricular region had been administered on September 9, 1947. No further treatment was deemed necessary at this examination.

On May 21, 1948, the patient's condition remained unchanged. The oral mucosa and gingivae appeared to be in excellent condition.

On June 15, 1948, the patient had lost no more teeth. The upper left first permanent molar was beginning to erupt into the oral cavity. No further roentgenotherapy was indicated at this time.

Summary

The importance to the dentist of awareness of certain ulcerative lesions of the oral cavity which may reflect the presence of a serious, fundamental metabolic disorder has been stressed.

Three of the so-called xanthomatoses, Letterer-Siwe's disease, Schuller-Christian's disease and eosinophilic granuloma of bone have been discussed from a clinico-anatomic viewpoint.

Letterer-Siwe's disease is apparently the more acute, septic form, fatal within a matter of weeks or months. It usually occurs in infants or in children before the age of 4. Histologically it is considered to be a nonlipoid histiocytosis. The lesions may occur in bone or soft tissue.

Schuller-Christian's disease is the more chronic variant. If extensive involvement of the bones of the skull occurs, the Christian triad of diabetes insipidus, exophthalmos and calvarial bone defects may be evident. Serious lesions of soft tissue may occur. Histologically it is considered to be a lipogranulomatosis.

Eosinophilic granuloma of bone is the most benign variant of the three. The lesions are localized much more and appear to form only in the skeleton, usually in a single bone. Histologically the lesion is considered to be a chronic granuloma of bone.

A case of eosinophilic granuloma of bone has been presented. Lesions were present in the skull and left mandible. Surgical curettage and roentgenotherapy were used as therapeutic measures. Approximately one month after treatment the lesion in the mandible was slightly larger. Otherwise no progression of the disease was noticeable.—*Department of Oral Surgery, College of Dentistry, University of California.*

UMI

ADAMANTINOMA OF THE MANDIBLE: REPORT OF CASE

Joseph E. Schaefer, M.D., D.D.S.,
Chicago

A WHITE WOMAN, aged 55, desired treatment of a marked swelling of the right side of the face, which had been present for twelve years. During the previous three years it had increased markedly in size.

Seven years previously this mass had been diagnosed as an adamantinoma and the tumor was removed intra-orally by curettage. Radium was inserted in the bone cavity. This treatment apparently gave the patient relief for about seven years, at which time the swelling of her face recurred.

The family history, in regard to this condition, was negative.

Examination.—Examination revealed a marked deformity of the right side of the face. Roentgenographically a large region of bone destruction was evident in the right mandible. The mass was spherical in shape with a radiolucent center. The circumference of the sphere was definitely radiopaque. One would interpret this tumor mass as having a central soft core covered by cortical bone.

Laboratory Examination.—Microscopic study of a biopsy section taken from the central mass of the tumor gave the typical cellular structure of an adamantinoma. A blood count revealed: hemoglobin 98 per cent; erythrocytes 4,000,000; leukocytes 8,500. A test of the urine was negative for albumin and sugar. The serology was negative.

Chief of maxillofacial surgery, Cook County Hospital, Chicago; and professor of oral surgery, Dental School, Northwestern University, Chicago.

Fig. 1.—Left: Marked deformity of the mandible because of tumor growth. Right: Appearance after resectioning of one-half of mandible

Fig. 2.—Left: Roentgenogram showing destructive process by adamantinoma of right mandible. Right: Right mandible has been resectioned and replaced by cartilage and rib graft. The bony portion of the rib graft is barely discernible at point of wire suture. The cartilaginous portion is not sufficiently radiopaque to show its position

Treatment.—On October 5, 1946, the patient was admitted to the hospital for removal of one-half of the mandible.

With the patient under ether anesthesia, the right external carotid was exposed and ligated. An incision was made along the lower border of the mandible from the angle of the jaw to the midline. The bone was dissected free from the soft tissues, and a Gigli saw was passed circumferentially around the body of the mandible in the right cuspid region.

An osteotomy was done at this time. The freed fragment was grasped with heavy forceps and the half of mandible was disarticulated from the temporomandibular fossa and removed. The floor of the mouth was reconstructed and a plastic ramus made of acrylic was inserted between the planes of the masseter and internal pterygoid muscles. The deep tissues of the neck were closed with catgut, and the skin with black silk.

Postoperatively the patient was placed on a morphine sedative and 20,000 units of penicillin every three hours.

The patient made an uneventful recovery.

Second Operation.—Nine months later the defect of the right mandible was replaced by a section of the seventh rib.

On August 21, 1947, with the aid of ether anesthesia, the site of the missing half of the mandible was opened up through the old submaxillary incision, and the acrylic form was removed from the muscle planes. The seventh rib, inclusive of the costal cartilage for angular restoration of the mandible, was dissected out of the right thoracic wall and inserted in the prepared bed for mandibular restoration. The cartilaginous end of the rib was passed between the muscle planes of the masseter and pterygoid well into the site of the temporomandibular joint.

The bony section of the rib was brought in contact with the exposed left half of the mandible and wired to it.

The soft tissues were closed with catgut sutures, and the skin was closed with black silk.

It is unfortunate that the density of the cartilage transplant is such that it is not demonstrated by the roentgenogram (Fig. 2, right). However, one can visualize the bony portion of the transplanted rib with its wire suture.

Postoperatively a plaster head bandage was applied for fixation because the patient was edentulous.

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Results.—The results of resectioning of the mandible and replacement by cartilage and rib graft are shown in Figures 1, right, and 2, right. Further plastic work is desirable to gain a better contour of the face. I have in mind a free epithelial fat transplant taken from the abdominal wall.

Functionally, the patient seems quite satisfied.—*804 West Seventy-Ninth Street.*

Interosseous Wiring in the Treatment of Fractures of the Mandible. Stuart Gordon, in *Arch. Surg.* 55:660, 1947.

Interosseous wiring as a method of treatment in suitable fractures of the mandible has been used by the author in 48 fractures in 46 patients.

Wire suture of the fractured mandible is applicable in fractures of the edentulous mandible, fractures having an edentulous posterior fragment, multiple fractures (for stabilization of the main fracture), bilateral fracture through the mental foramina with downward displacement of the central fragments, gun (or shell) wounds (for stabilization when a portion is missing) and in fractures at the base of the condyle with displacement. The procedure used by the author is as follows:

An incision is made below the mandibular line. No attempt is made to protect the inframandibular branch of the facial nerve, as recovery uniformly has followed its injury. The fracture ends are freed of soft tissue on both surfaces for about ¾ inch. Two holes are drilled in each end. . . . A high speed drill should not be used. Twenty-six gauge stainless steel wire is threaded through the upper two holes as a simple suture. It is not tightened until the other wire is in place. It was found that some degree of displacement of the posterior fragment recurred if the lower wire was also used as a simple suture. Therefore, this wire is placed as a figure 8, with the crossed portion under the edge of the fragment not tending to become displaced. This prevents any postoperative shift. The wires are tightened with the fracture reduced. As it is believed that the least possible movement at a fracture line, particularly when foreign material is present, aids the development of solid union with a minimum of complication, intra-oral fixation was used as well in 43 patients, pins and a Gunning splint in 1 patient each and no secondary fixation was used in the forty-sixth patient.

If a tooth in the line of fracture was rather loose or fractured, or had a denuded root in the fracture line, it was extracted before the incision was made. If possible, an intra-oral dental roentgenogram was taken, since the information obtained from it is of more value than that obtained from a large roentgenogram.

Six of the 48 fractures were simple. Postoperative infection did not develop in any of these. There were 10 postoperative infections in the remaining 42 compound fractures wired. Two of these were serious, resulting in osteomyelitis with sequestration in one case and nonunion in the other. One of the other 8 infections produced abscesses involving soft tissue only, which had to be drained but caused no further damage.

Union occurred in the cases without infection in an average of forty-four days. In cases with infection union occurred in an average of fifty-four days.

In the 2 cases of condylar fracture, wiring was done in order to reduce the fracture and to maintain the position. It was thought by the author that the functional result obtained was no better than that obtained from the usual methods of treatment, so open reductions were abandoned in this type of fracture.

It was thought from the experience obtained in these cases that the use of interosseous wiring in the treatment of fractures of the mandible was of value in maintaining edentulous fragments in anatomic position; in stabilizing a mandible when a portion was missing or when multiple fractures were present; and in maintaining accurate reduction of the central fragment when fractures were present in both mental regions; but it was of questionable value in the treatment of fractures of the condylar process. Interosseous wiring makes it possible to obtain and maintain a more accurate reduction of the fracture than that obtained by any other applicable method of therapy. This method should never be used when acute infection is present, but its use is not contraindicated in compound fractures free of clinical signs and symptoms of infection. —John E. Karabin, in International Abstracts of Surgery, *Surg., Gynec. & Obst.* 86:434 (May) 1948.

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TUBERCULOUS OSTEOMYELITIS OF THE MANDIBLE WITH REPORT OF CASE

Orion H. Stuteville, D.D.S., M.D.,
and Franklin F. Hulswit, D.D.S.,
Chicago

TUBERCULOUS osteomyelitis of the mandible is rather rare. However, those cases that have been reported in the literature indicate that infection of the jaws may occur in many ways. Stein[1] reported a case where entrance of infection was through a carious tooth in a patient with positive sputum. Partsch[2,3] demonstrated that tubercle bacilli were present in the periodontal tissue near the apex of the root; this author described for the first time tuberculous periodontitis in 1932. Thoma[4] described another mode of entrance by way of hypertrophied gingival margins covering partially erupted third molars. Burman and Jonsson[5] reported 15 cases of tuberculosis of the mouth following tooth extraction. Foldi[6] demonstrated microscopic evidence of tuberculous changes in a granuloma at the apex of an extracted tooth. Chapotel[7] stated that through hematogenous channels a diffuse form of osteomyelitis is produced. Stein[8] wrote on newer

From the Department of Oral Surgery, Cook County Hospital, Chicago.

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2. Partsch, C., Die Chronische Wurzelhautentzündung. Deutsche Zahnheilkunde in Vorträgen, Leipzig, 1904.
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8. Stein, George, Newer Aspects of the Problem of Focal Infection. *Am. J. Orthodont. & Oral Surg.* (Oral Surg. Sec.) 28:28 (January) 1942.

Fig. 1—Roentgenogram showing region of rarefaction with sclerosis

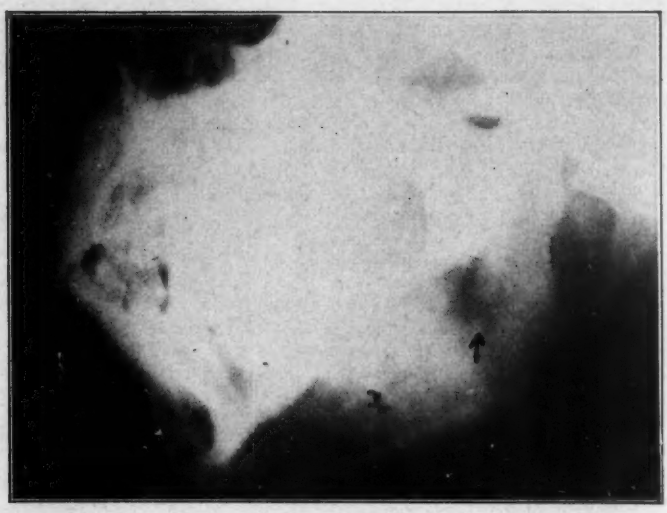

Fig. 2.—Roentgenogram showing operative defect

aspects of focal infection in 1942 and based his work on personal investigations and experiments.

Report of Case

A Negro woman, aged 30, was admitted to the Cook County Hospital on August 14, 1947, as a transfer patient from the Municipal Tuberculosis Sanitorium, for treatment of a draining fistula at the left angle of the mandible of twenty months' duration.

Examination.—Physical examination showed the patient to have advanced pulmonary tuberculosis with a phthisic appearance of the chest, hypotension, a blood pressure of 100/70, dyspnea, elevated temperature and an underweight condition. There was a firm enlargement inferior to the left angle of the mandible measuring 5 cm. in diameter, from which a yellowish, thick discharge could be expressed. Laboratory findings were essentially negative, except for a positive sputum.

Roentgenograms of the chest taken August 25, 1947, revealed dense, mottled infiltrations involving both lung fields, a more or less dense opacity involving the left midlung field and a suggestion of cavitation in the right infraclavicular region. Roentgenographic examination of the mandible on August 14, 1947, showed a region of radiolucence at the left angle with evidence of sclerosis around it. The margins of the ramus showed slight irregularity with evidence of increased density and sclerosis of the coronoid process suggesting changes compatible with an old chronic osteomyelitis (Fig. 1).

Past History.—In the early part of February, 1946, the patient had experienced pain and swelling on the left side of the face, with abscess formation and spontaneous drainage extraorally. No treatment was sought until March 1, 1946, at which time the patient came to the Cook County Hospital oral surgery clinic where a diagnosis of osteomyelitis of the mandible was made. It was judged to be the result of an infection of six months' duration which began as a pericoronitis around the lower left third molar.

Anteroposterior and lateral roentgenograms of the mandible taken at this time revealed swelling of soft tissue about the ramus and temporomandibular joint. There was evidence of mottled destruction at the lateral aspect of the ramus. The lateral view revealed a round opacity with

a region of radiolucence just inferior to the posterior root of the lower left third molar, which contained a large carious lesion in the crown.

On March 2, 1946, incision and adequate drainage was established under local anesthesia. The patient returned weekly for a change of dressings, and the abscessed tooth was extracted on April 5, 1946. On April 9 a roentgenogram of the left mandible revealed evidence of a rarefied region in the lateral view with sclerosis about it, indicating an infectious process of rather chronic nature. The patient failed to return.

On November 7, 1946, she was admitted to the obstetrical department of the Cook County Hospital. During confinement previous to delivery, an oral surgery consultation was requested. Examination at this time showed soft tissue swelling around the left ramus and temporomandibular joint, with a considerable amount of extra-oral drainage.

After an uneventful delivery of a normal infant, the patient was discharged without treatment of her infected jaw. There was no contact with the patient from this time until August 14, 1947. The patient stated that in April, 1947, she was admitted to the Municipal Tuberculosis Sanitorium with a diagnosis of active pulmonary tuberculosis.

Diagnosis.—A diagnosis was made of tuberculous osteomyelitis of the mandible, and on September 18, 1947, a radical sequestrectomy was performed.

Fig. 3.—Postoperative photograph showing region of healing and point where fistula was present

Operation.—With the patient under local anesthesia, a 7 cm. incision was made inferior to the left lower border of the mandible, extending from the angle to midway up the ramus. The soft tissues were retracted and the lower border and buccal surface of the mandible exposed. With the use of curettes and rongeurs the buccal plate was removed exposing an area of bony degeneration at the angle and anterior surface of the ramus. The infected bone was removed until a good bleeding surface was obtained, leaving the lingual plate intact. A soft rubber drain was inserted extending from the diseased region extra-orally, soft tissues were replaced and the wound was closed with interrupted black silk sutures.

A gross description of the overlying soft tissues indicated complete obliteration of normal anatomic structures and replacement by pearly gray, partially avascular, fibrosed tissues. The diseased bone had a spongy, grayish, avascular appearance with a whitish, stony consistency in the regions of sclerosis. Microscopic sections of the infected bone revealed chronic osteomyelitis.

Postoperative Treatment.—The postoperative management consisted of: (1) complete immobilization of the soft tissues by the application of a tight pressure bandage over the wound and fixation of the teeth in occlusion by means of Ivy loops and intermaxillary wiring; (2) adequate high caloric liquid diet, with 300 Gm. of protein and vitamins C and B complex added; (3) chemotherapy consisting of 30,000 units of penicillin every three hours, started seventy-two hours preoperatively and given for two weeks postoperatively, and (4) proper oral hygiene in addition to hydrogen peroxide mouth washes four times a day.

Course.—The postoperative course was uneventful. The sutures were removed on the fourth postoperative day and a fresh pressure dressing applied. Ten days postoperatively the drain was removed with all evidence of drainage subsiding two days later. On the twenty-fifth postoperative day the intermaxillary wiring was removed and the patient was placed on an adequate soft diet. Postoperative roentgenograms taken October 14, 1947, revealed a large rarefied region of cavitation present at the left angle of the mandible (Fig. 2). A profile photograph taken on the same date demonstrated the region of healing at the lower border of the mandible with no evidence of drainage (Fig. 3). The patient was sent back to the Municipal Tuberculosis Sanitorium for further treatment of her affected lung.

Fig. 4.—Roentgenogram taken three months postoperatively showing defect partially repaired

Three months postoperatively, January 29, 1948, the patient was returned to the oral surgery clinic for a checkup. Examination showed no evidence of recurrent swelling or discharge. Roentgenograms of the mandible revealed definite evidence of beginning calcification at the previous surgical site (Fig. 4).

Discussion

As indicated in the introduction, tuberculous osteomyelitis of the jaws may take place either by implantation or hematogenous routes. This case was believed to be caused by the implantation of tuberculous organisms from a positive sputum in the bone by way of a markedly carious, partially erupted lower third molar. We feel that although no diagnosis of lung pathology had been made at the time of the original dental infection, the patient had, at this early date, an active pulmonary tuberculosis. Consequently, even though the infected third molar was extracted, no healing ensued because of the presence of the implanted opportunist (tubercle bacillus) and the lowered resistance of the patient. Therefore, the treatment of this debilitated individual consisted of producing the best possible conditions for healing. This was accomplished by complete elimination of the diseased bony cavity, rest and immobilization of the tissues and a supportive diet.

Summary

The evidence points to a true tuberculous osteomyelitis even though it was impossible to demonstrate the presence of the tubercle bacillus in the lesion by means of cultures, smears or microscopic sections.

Naso-Endotracheal Intubation with Cyclopropane Anesthesia for Oropharyngeal Surgery. H. L. Harang, in *Anesth. & Analg.* 27:152 (May-June) 1948.

Summary

Cyclopropane fulfills all the requirements of an anesthetic agent for oropharyngeal surgery. It has a potency sufficient to carry anesthesia to a plane deep enough for relaxation of intrinsic and extrinsic muscles of the larynx with depression of reflexes. There is no anoxia or hypoxia because of an increase of 55 per cent oxygen above other gas anesthetics.

The above properties of the anesthetic agent, combined with the skill of the anesthetist, permits the establishment of a controlled airway throughout the operation. The danger of aspirating foreign bodies is considerably lessened, and the anesthetist's equipment is out of the surgeon's field of operation.

It has been shown through careful study and preparation of the structures involving the pharynx and larynx that a blind intubation may be successfully accomplished without trauma. The procedure for endotracheal intubation takes less than two minutes and not more than five. A rapid and pleasant induction is ensured. An established airway is maintained through adequate relaxation of the muscles.

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EOSINOPHILIC GRANULOMA OF THE MANDIBLE: REPORT OF CASE

Wilson R. Conran, D.D.S.,
Hartford, Conn.

A HIGH-SCHOOL BOY, aged 17, was referred to the author, bringing with him roentgenograms taken at his local hospital. He complained of pain and marked swelling in the left side of the cheek and mandible, some tenderness and looseness of the lower left second and third molars. There had been no family history of any similar trouble.

Physical Examination.—Examination of the chest was negative. The heart was not enlarged and there were no murmurs. The pulse rate was 76, and the blood pressure was 115/70.

Roentgenographic Examination.—Roentgenograms revealed a large region of destruction extending from the distal portion of the third molar, around the roots of the second molar (the first molar was missing), then down and forward and well below the apices of the first and second bicuspids up to the distal proximal space of the cuspid (Fig. 1, left). The lesion extended to the lower border of the mandible. The roentgenologist who had made the roentgenograms for the boy diagnosed it as "possibility of osteogenic sarcoma." Inasmuch as the outline was not definite, the author had additional roentgenograms taken after the first roentgenologist's diagnosis. The report was as follows:

"On October 8, 1947, examination of the mandible shows a large oval shaped cystlike area of rarefaction almost 4 cm. in size in the left molar and premolar regions. Almost the entire thickness of the mandible is involved by the pathologic process so that a pathologic fracture easily could occur. Anteriorly the cystic process appears to extend entirely through the bone margin. There is slight mottling throughout the pathologic area. The apices of the molar teeth are involved in the cystic area but the apices of the bicuspid teeth do not appear to be involved.

"Conclusions: Large odontogenic cyst or tumor involving the left side of the mandible in the molar and premolar region."

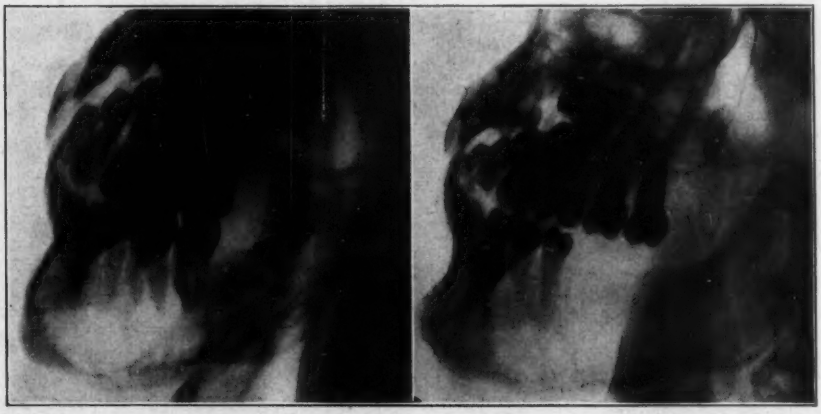

Fig. 1.—Lateral jaw roentgenograms. Left: Extensive destructive lesion of eosinophilic granuloma. Right: Progress of regeneration of bone seven weeks after operation

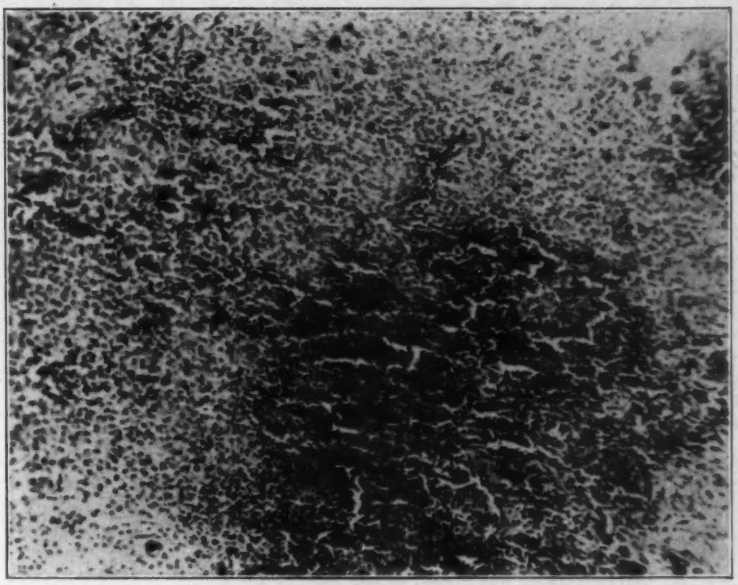

Fig. 2.—Low power photomicrograph of tissue section

Inasmuch as the region seemed to involve the two broken down molar teeth with considerable destruction of bone, the author diagnosed it as radicular cyst of the mandible.

Operative Procedure.—With the patient under thiopental sodium anesthesia, an incision was made 0.5 cm. distal to the border of the third molar forward to the distal border of the cuspid. The gum tissue was retracted, this bony prominence, which was very thin and not unlike parchment, was removed and the second and third molars were extracted. The membrane was attached to the gingiva of both of these teeth, but the tissue was very friable and it was impossible to remove it completely. It extended down to the roof of the mandibular canal tipping down well below the apices of the two bicuspids. The bicuspids were vital and there was a considerable amount of solid bone between them and what the author considered a cystic region.

The membrane was enucleated, many small fragments of the tissue were removed and the cavity was swabbed with 7 per cent chromic acid to slough any material which had been overlooked in the process. The region then was dried out and examined again and dusted well with sulfadiazine powder. The gum flap was brought back in position without any sutures.

Laboratory Findings.—The fragments of tissue were sent to the Hartford Hospital laboratory for examination. The laboratory report did not confirm the radicular cyst, but proved it to be eosinophilic granuloma, which is rare and generally occurs in very young persons.

Macroscopically, the region was made up of two lower teeth and three irregular, grayish white fragments of tough fiber-like tissue, each having one ragged side.

A microscopic section showed tissue to be composed of masses of eosinophilic polymorphonuclear leukocytes and mononuclear cells arranged in small, round and spindle shaped, reticular connective tissue cells in irregular masses (Fig 2). In the mononuclear cells eosinophilic granules were extremely large, and along the margin of the tumor there appeared to be a thin fibroperiosteal layer and a few bone spicules. Cells were separated occasionally by granular precipi-

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tated edematous fluid and were interspersed with foci of hemorrhage and foci of fibrinous necrosis. The pathologic picture was that of eosinophilic granuloma.

From the little literature available on this disease,[1-6] it is evident that laboratory findings are the only means of determining the type of this tissue.

There is always a question of additional lesions either in the long bones or pelvic bones which should be examined by roentgenography. A lateral roentgenogram of the skull and single ones of each tibia, and fibula, each forearm, and of the pelvis and upper femora showed no evidence of any bony abnormality.

Second Roentgenographic Examination.—On December 1, 1947, re-examination of the left side of the mandible by roentgenography, for comparison with the previous examination on October 8, 1947, showed evidence of an operative procedure with removal of the two remaining lower left molar teeth (Fig. 1, right). The pathologic region in the mandible apparently had been curetted, and the bony defect was slightly larger at this time than at the previous examination. However, there had been some filling in with new bone production so that the bone structure in the pathologic region had gained a more solid appearance.

Result.—The patient made an uneventful recovery and has experienced no discomfort.—*750 Main Street.*

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2. Bailey, J.W., and Freis, E.D., Eosinophilic Granuloma of Bone with Manifestations in the Jaw. *J.A.D.A.* 31:91 (January) 1944.
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Pterygomandibular Abscess Confused with Acute Peritonsillar Abscess. With Report of Case. Samuel Zurik (Lt. Comdr., M.C., USN) and Mitchell M. Tanner (Lt. Comdr., D.C., USNR), in *U. S. Nav. M. Bull.* 46:1909 (December) 1946.

A case history of a member of the Women's Reserve, with a pterygomandibular abscess confused with acute peritonsillar abscess, is reported. The chief complaint was sore throat and difficulty in swallowing. The temperature was 100.2 F. Examination of the pharynx revealed marked swelling and infection of the right anterior pillar of the fauces with some edema and displacement of the uvula to the opposite side. The case was diagnosed as acute peritonsillar abscess and was treated with sulfonamides and hot saline irrigations, but the symptoms were not relieved. Shortly thereafter the abscess on the anterior pillar became more circumscribed and fluctuant, but in the right pterygomandibular space a small fistulous opening appeared. Pressure over the anterior pillar abscess evoked a sanguinopurulent discharge, and a probe was introduced through the fistulous opening to the abscess in the anterior pillar. An incision was made over the path of the probe, and a copious purulent discharge occurred containing two particles of tooth structure. The abscess was evacuated and packed. The patient had had a lower right third molar extracted one month prior to the onset of symptoms, and it was believed that fragments of the tooth had become dislodged and were imbedded in the pterygomandibular fossa.—*Quart. Rev. Otorhinolaryng. & Bronch.-esoph.* Vol. 6, June, 1947.

PHOSPHOROUS NECROSIS OF THE MANDIBLE: REPORT OF TWO CASES

B. G. Wakefield, D.D.S.,
Buffalo, N. Y.

THE TWO CASES presented are believed to be of general interest because the first one was the first case of phosphorous necrosis to be seen by anyone in western New York State for more than twenty years; after this three similar cases from the same source were observed within a period of one year from its occurrence.

Case 1

A man, aged 40, who always had been in good health, gave a negative personal and family history for any similar ailment.

His illness began July 8, 1941, when after sixteen years of employment in the manufacture of crude phosphorus, he had developed painful symptoms in his lower jaw, the teeth of which were involved with pyorrhea. These symptoms became so extreme that his dentist decided on the removal of all lower teeth. This served only to aggravate his condition which became decidedly worse until, in desperation, he sought help in a veterans hospital. Here he was put on the general surgical service, and a diagnosis of osteomyelitis of the mandible was made. The correct diagnosis later was found to be phosphorous necrosis of the mandible.

The general surgeon decided on a resection of the left side of the mandible, where roentgenographic evidence of necrosis had been seen, although his pain was bilateral. The resection included the mandible from the left cuspid to a point midway between the angle and the articulation.

His condition became worse, and finally the roentgenograms showed breaking down of the right side, whereupon it was decided to resect the remainder of the mandible. The patient rebelled against this, signed his own discharge and went home to consult his family physician who referred him to us on October 21, 1941.

Examination.—The patient was admitted to the Millard Fillmore Hospital on October 21, and examination showed him to be very ill, with a temperature of only 99 F., but with excruciat-

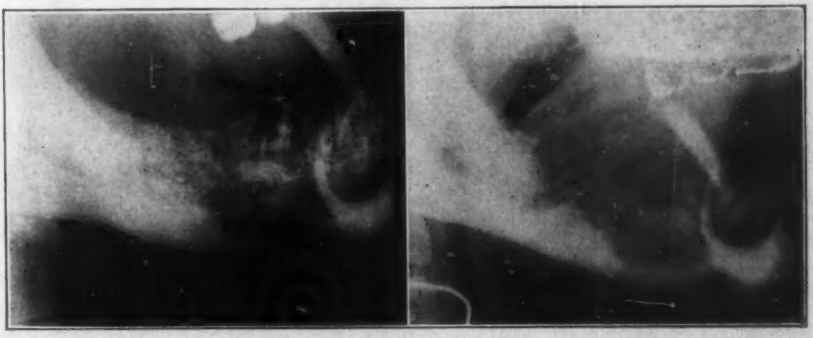

Fig. 1, Case 1.—Left: Resection of the left side of the mandible and involvement of the right side (October 22, 1941). Right: Further decalcification is evident but no further extension of necrosis (February 6, 1942)

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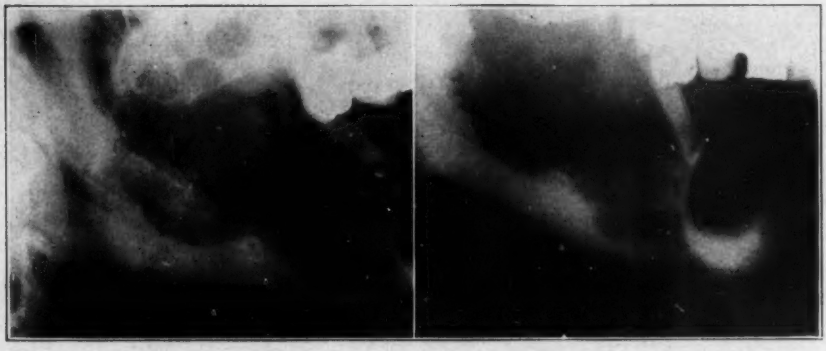

Fig. 2, Case 1.—Left: Sequestrum (March 9 1942). Right: Region after removal of sequestrum (March 15, 1942)

ing pain. An ugly wound beneath the left mandible was draining foul, pungent material. Inside the mouth, there was also drainage in the resected region. The mucoperiosteal tissue over the remainder of the mandible was cyanosed in appearance, raised, tender and already had some perforations with inadequate drainage. Some deformity existed as a result of the resection, and the mandible had shifted toward the resected side.

Roentgenograms were made which revealed an involvement of the body of the right mandible down to the lower border (Fig. 1, left). Skeletal roentgenograms showed nothing abnormal when a survey was made on November 4, 1941. Films of the skeletal parts including the right shoulder girdle, thoracic cage, dorsal and lumbar spine, right knee and right forearm revealed no definite evidence of bone or joint pathology. The skeletal parts shown in these regions appeared to be within normal limits for the patient's age of 43.

Treatment.—An incision was made over the crest of the ridge of the remaining lower jaw in order to reflect the mucoperiosteum away from the bone for complete unhampered drainage. After irrigation it was dressed with lubricated ½ inch gauze, and this was repeated daily, whereupon the pain lessened promptly and the patient improved. While the bone continued to be decalcified, necrosis did not extend further after adequate drainage was established and maintained (Fig. 1, right).

Sulfathiazole was given with sodium bicarbonate from October 23 to 29. Various irrigating solutions were tried but best results seemed to be obtained by the use of saline to which a few crystals of copper sulfate were added, just sufficient to discolor the solution slightly. Its value, no doubt, was in its ability to combine with phosphorus. Empirin compound (Burroughs Wellcome) with codeine and Nembutal (Abbott) were used to control pain, with an occasional ¼ gr. of morphine sulfate.

All extensive surgery was avoided. Sequestrums (Fig. 2, left) were removed (Fig. 2, right) only when they were freed completely from surrounding good bone. The time required for sequestration was many times greater than in cases of ordinary osteomyelitis, as though bacterial action was being resisted. It was found also that when some sequestrums were removed there was an interlocking of vital and dead bone. The sequestrums were hard and irregular, much like clinkers from a coal furnace, and in each case possessed a very pungent odor. All tests on these sequestrums for phosphorus were negative. This may have been caused by the flushing-out action of the drainage and irrigations, or possibly was a result of the combining action of the copper sulfate. It is also true that no tests yet conceived are capable of detecting small amounts of phosphorus.

A test of the urine on October 24 showed a specific gravity of 1.021; there was an acid reaction with a trace of albumin, and no leukocytes or red cells were present.

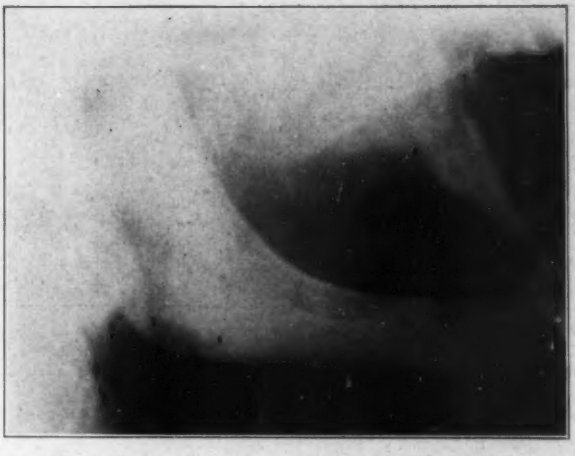

Fig. 3, Case 1.—Regeneration of right jaw (May 8, 1942)

The blood count on October 23 showed leukocytes 9,300 per cubic millimeter, with neutrophils 72 per cent; lymphocytes 20 per cent; eosinophils 5 per cent; basophils 2 per cent, and myelocytes 1 per cent.

The blood picture did not vary greatly during his illness.

In spite of severe illness and drainage, the temperature remained very low. For example, from his first day in the hospital the highest daily temperatures ran as follows: 99.0; 100.0; 99.5; 100.0; 98.6; 100.0; 98.6; 98.6, and 98.6 F. On two occasions during a period of sequestration, his temperature did reach 100.2 F., which of course is in contrast to ordinary osteomyelitis. He was discharged from the hospital on November 16, 1941; after this he was seen at office calls until his final discharge on May 8, 1942.

Progress continued until regeneration was complete (Fig. 3), and the patient was discharged with no additional deformity or loss of function. Dentures have been made since that time which serve well for esthetic purposes but not for mastication in view of the lost mandible on the left side.

Case 2

The unusual factor of interest in this case is its bilateral involvement, beginning at different times but under identical circumstances, after the patient had spent approximately ten years as an employee in the manufacture of crude phosphorus.

The patient, a man 25 years of age, gave an irrelevant negative personal and family history, in relation to this ailment, on his first visit to the office on December 15, 1941. His illness had started three days before his visit to the office. At that time he had noticed tenderness and steady pain in the left mandibular third molar region. The latter tooth was very tender to percussion and occlusion. The pain did not yield to the usual sedation.

Examination.—Clinically, the patient did not show extra-oral swelling, but the mucosa in the left molar region and slightly distal to third molar appeared congested and raised, similar to the condition seen in early osteomyelitis. No trismus was present at the time. A pocket distal to the third molar tooth appeared to have existed over a period of time and seemed to be draining. The patient acted and looked toxic, but his temperature was only 99.5 F. in spite of the involvement.

Treatment.—Lateral jaw roentgenograms were made and the pocket was irrigated and treated. The patient was placed on sulfathiazole therapy and hourly hot irrigations, intra-orally, and

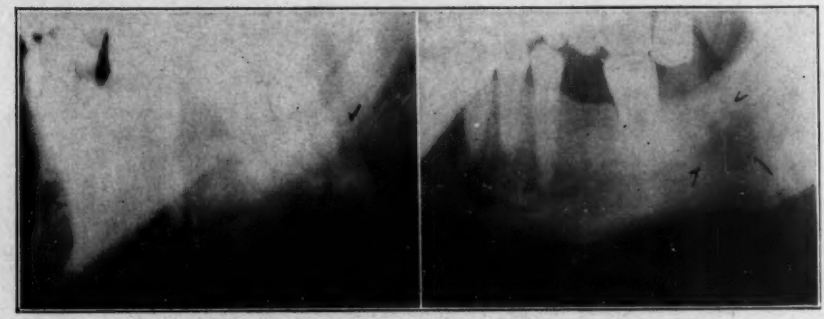

Fig. 4, Case 2.—Left: Left jaw showing pocket distal to the third molar tooth leading to the region of bone necrosis (December 15, 1941). Right: Sequestrum in the third molar socket. Pain in the second molar region was unbearable (January 29, 1942)

cold packs extra-orally. Because he was from out of town, he was requested to consult the dentist at his plant, and to return within at least four days if symptoms persisted.

The roentgenogram (Fig. 4, left) revealed a large region of bone necrosis distal to and below the third molar. We became suspicious of phosphorous necrosis. When he returned on December 19, his pain had increased to an unbearable extent, and the removal of the third molar tooth, with the use of general anesthesia, became necessary. The region was cleaned out thoroughly and dressed with a lubricated dressing (Fig. 4, right) and redressed and irrigated daily.

The patient became quite comfortable for a short while, but five weeks later the second molar and second bicuspid became painful. Pain in the molar was so severe that it required extraction (Fig. 5, left), and the third molar socket had to be freed of sequestrating bone. Still later, before checking the condition the second bicuspid required removal. The pain was so intense and unyielding to sedation that on January 14, 1942, a mandibular alcohol block was resorted to with success.

Bilateral Involvement.—Five weeks from the original onset in the left third molar region, similar symptoms began on the right side, and a lateral jaw roentgenogram was made (Fig. 6,

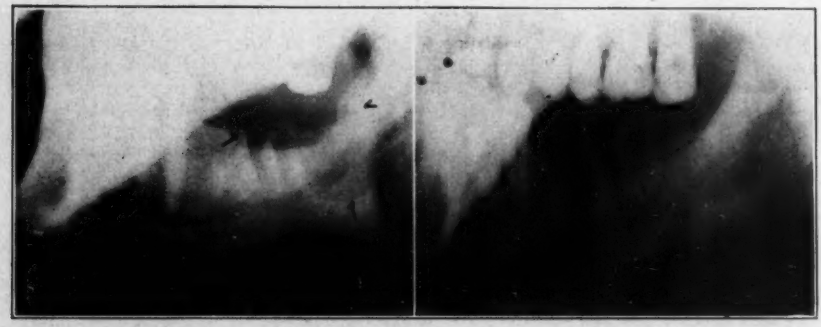

Fig. 5, Case 2.—Left: Left jaw after extraction of second molar tooth and removal of sequestrum in the third molar socket (March 19, 1942). Right: Regeneration of the left mandible (October 5, 1943)

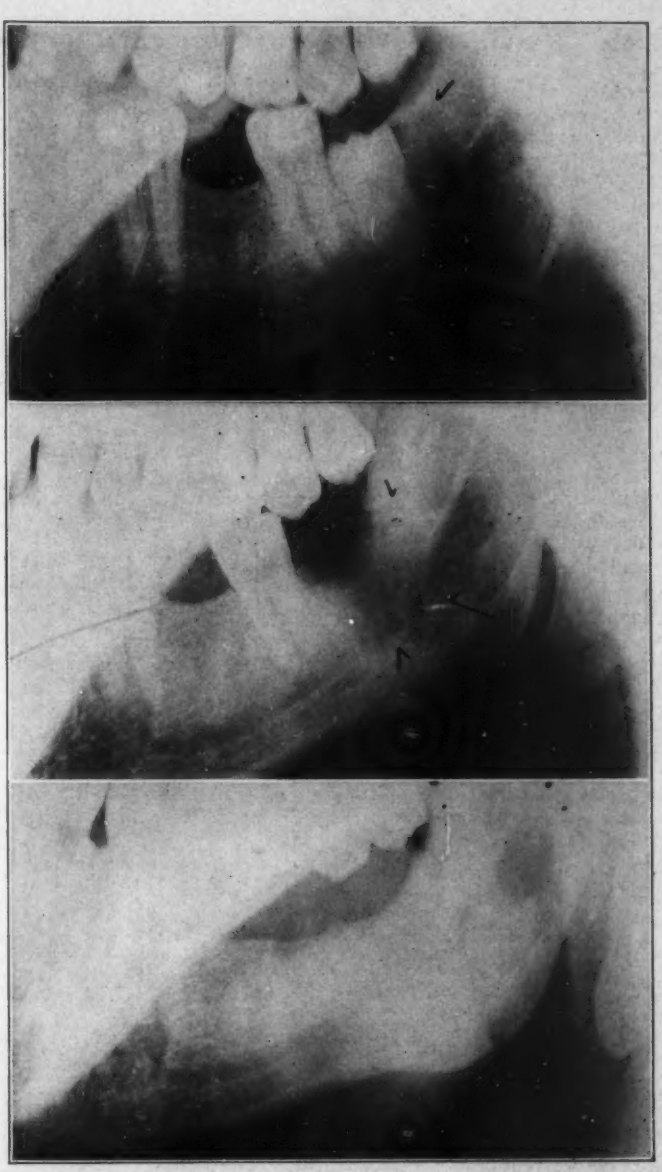

Fig. 6, Case 2.—Top: Right jaw (January 21, 1942) showing similar necrosis distal to the third molar tooth. Center: Right jaw after removal of the third molar tooth (March 9, 1942). Bottom: Right jaw after removal of second molar tooth, showing regeneration of right mandible (December 11, 1942)

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top.) It revealed similar necrosis around the unerupted third molar, and the latter was removed, the region cleaned out and the same routine of dressing carried on.

Two months later, pain in the second molar, although it was roentgenographically negative (Fig. 6, center), became unbearable and the tooth was removed. The pain gradually subsided, and the left side was already on the way toward recovery.

The final roentgenogram of the right side (Fig. 6, bottom) was made on November 11, 1942, and showed complete regeneration. The left side required more time, and the final roentgenogram (Fig. 5, right) showing complete regeneration was taken on October 5, 1943.

It was learned in previous cases that a few crystals of copper sulfate, sufficient to color slightly the irrigating saline, was helpful in checking this condition. This action is probably caused by its combining action with phosphorus. Such a solution was used from the beginning in this case.

Conclusion

It seems that patients working with phosphorus over a period of time build up a point of tolerance. Phosphorous necrosis appears to be accumulative, and occurs when one's saturation tolerance has been exceeded and where there is some portal of entry. Such a portal would seem to be granulation surfaces, open vascular tissue in the mouth where saliva laden with phosphorus was retained, such as may be found in pyorrhea pockets, third molar flaps and extraction sockets while unhealed. Phosphorus workers should have rigid dental supervision with examinations three or four times yearly. Dental hygiene and effective home care must be maintained. In the event of extractions or other oral surgery, the worker should stay away from work until the oral tissues are healed completely.

Painful symptoms precede all others by a matter of days or weeks.

Roentgenographic evidence is far behind the actual progress of the disease.

Resections are contraindicated because the mandible has such regenerative power if the mucoperiosteum is protected and held out to contour. Conservative treatment in this, as in other osteomyelitic conditions of the mandible, seems likely to bring about the best results in regeneration.

Dilute copper sulfate solutions as irrigating mediums are helpful in checking the extension of phosphorous necrosis.

Drainage from phosphorous necrosis has a very foul, pungent odor. Free drainage and daily irrigations are essential to successful recovery.

Dental surgeons are better equipped to treat patients with this disease than general surgeons.

The usual sedation of opiates and barbiturates is inadequate in the early stages of this disease.

The low temperatures of patients with phosphorous necrosis are in contrast to those with osteomyelitis. It leads one to believe that sepsis is secondary and is resisted by the action of phosphorus.—*333 Linwood Avenue.*

AMERICAN SOCIETY OF ORAL SURGEONS

The thirtieth annual meeting of the American Society of Oral Surgeons will be held at the Stevens Hotel in Chicago, September 9 to 11, 1948. The secretary is Harry Bear, 1112 East Clay Street, Richmond 19, Va.

CALCIFIED ODONTOGENIC TUMOR (DENTINOMA) OF THE MANDIBLE: REPORT OF CASE

Robert G. Knapp, D.D.S.,
Utica, N. Y.

A WELL DEVELOPED, well nourished white man, aged 31, presented himself for examination on January 20, 1947. There was a marked hard swelling on the right side of the face extending from the lower border of the mandible anterior to the ear into the temporal fossa. At first glance, the appearance seemed to suggest acromegaly.

The patient reported that the lower right third molar had been removed, with subsequent difficulties. After the extraction many visits were made to the dentist. Intra-oral roentgenograms had revealed a radiopaque region resembling a sequestrum distal to the third molar socket. An attempt was made to remove this by the dentist, and fracture of the needle occurred during injection. The patient sought treatment from the author by referral after this difficulty.

Physical Examination.—The swollen region was very hard and dense on palpation. There was no discomfort to the patient on internal or external palpation. The temporomandibular joint was limited in movement. The patient was able to open his mouth about ¾ inch. Beyond this, normal movement of the mandible was difficult.

Roentgenographic Examination.—Intra-oral and extra-oral roentgenograms showed a large tumor of the mandible occupying the entire body of the ramus from the region of the third molar to the mandibular notch (Fig. 1, left).

Operation.—On September 19, 1947, the patient was admitted to Faxton Hospital, Utica. Premedication of morphine sulfate gr. 1/6 and atropine gr. 1/150 was given thirty minutes before surgery. Induction with nitrous oxide and oxygen followed by ether was the anesthetic used.

A black silk suture was inserted through the tongue and tied firmly to the mechanical mouth prop to keep the tongue well forward in the mouth. A Seldin throat pack was inserted at the junction of the hard and soft palates using a clockwise rotation to prevent the obstruction of the airway.

An incision was made distal to the third molar socket extending up the ramus to a point opposite the mandibular notch. The incision was continued anterior to the third molar socket

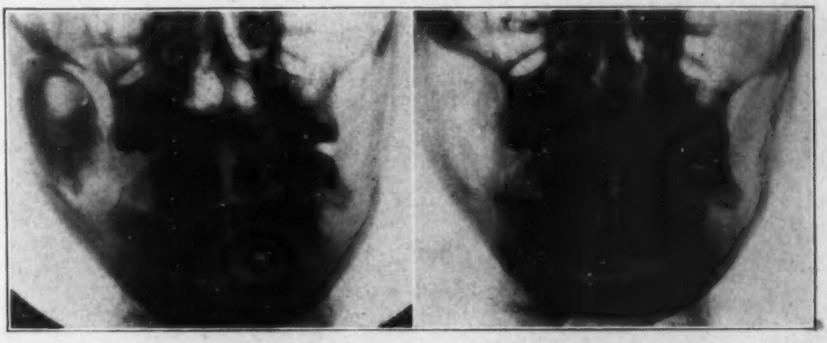

Fig. 1.—Postero-anterior roentgenograms of the ramus. Left: Dentinoma of the entire body of the ramus. Right: Postoperative view showing repair of the mandible, four months later

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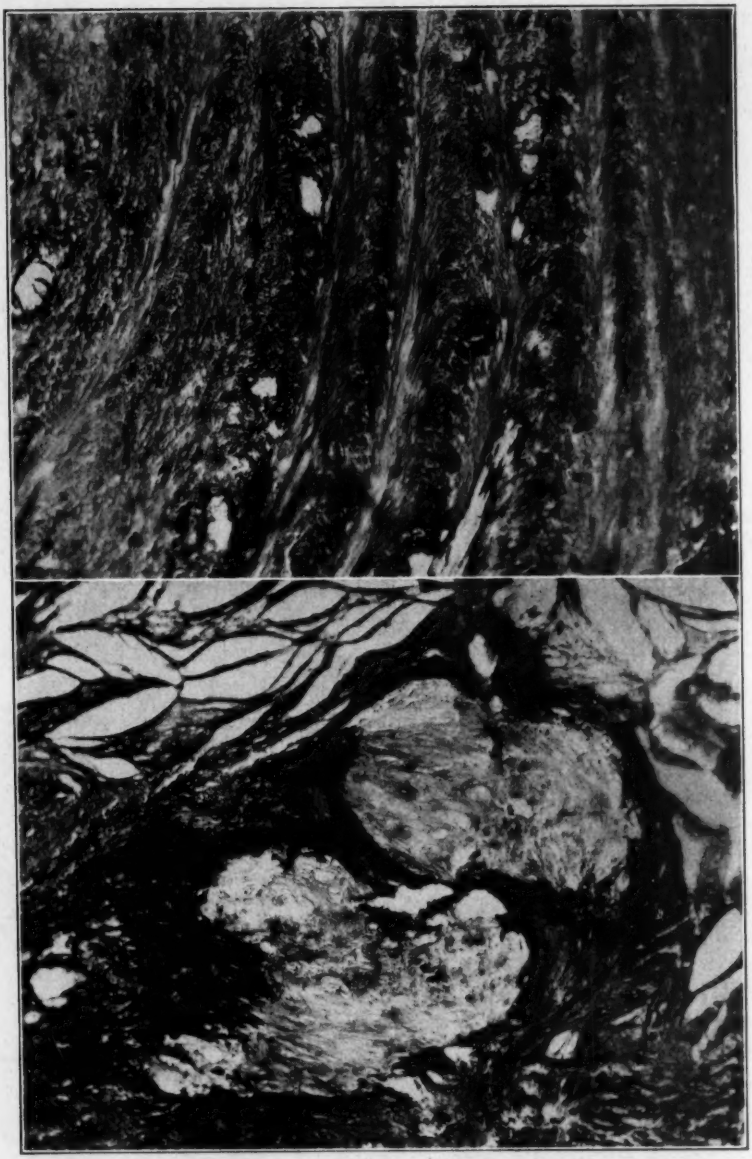

Fig. 2.—Photomicrographs. Above: Low power view of the section through the entire cyst showing calcareous deposits. Below: High power view of section through calcified region

Fig. 3.—Gross specimen of the tumor

over the crest of the mandible to the first bicuspid region. By using a periosteal elevator, a generous exposure of the entire region was accomplished. Mattress sutures were used on the buccal and lingual flaps for retraction, making it possible for the assistant to keep the region in excellent view.

The tumor was extremely hard and dense and measured approximately 6 cm. (Fig. 3). The outer surface had the appearance of cortical bone dimpled with small spots of soft tissue. It was encapsulated heavily as suspected from the radiolucent zone surrounding the tumor. Its complete removal was made possible by removing a small amount of bone on the buccal and anterior wall of the ramus. The region was dusted with sulfanilamide powder. The space was packed lightly with sterile petrolatum gauze. Black silk sutures were used to close incisions, allowing for the removal of the dressing and for irrigation. The specimen was sent to Kurt H. Thoma for study. He has confirmed the diagnosis of dentinoma (Fig. 2).

Postoperative Course.—The patient had an uneventful recovery. The following day he was ambulatory and pain was controlled with acetylsalicylic acid and codeine. On the third day, the dressing was removed and the cavity was irrigated with warm saline. A smaller dressing was inserted and changed twice a week until October 25, 1947. At this time, the patient was able to keep the region free from contamination simply by rinsing his mouth after meals. Postoperative progress was checked with roentgenograms which showed an early repair of the mandible (Fig. 1, right).

Conclusions.—This case demonstrates conclusively the importance of extra-oral roentgenograms. In the field of oral pathology the complete and detailed roentgenogram of the entire mandible or maxilla is essential for an accurate diagnosis.—*258 Genesee Street.*

OSTEOMYELITIS OF THE RAMUS OF THE MANDIBLE: REPORT OF CASE

Ralph W. Taylor, D.D.S.,
Alameda, Calif.

A WHITE MAN, aged 28, was admitted to the hospital in February, 1944, because of a draining fistula in the right cheek.

History.—After the removal of the right mandibular third molar tooth in June, 1943, an osteitis had developed in the alveolus. The patient received treatment for approximately one month. Several weeks after the extraction, swelling and tenderness over the right condyle was noted. The swelling increased, pain became more severe and for several days the patient was quite uncomfortable. Then the lesion ruptured spontaneously externally with a free flow of pus and alleviation of painful symptoms.

The fistula continued to drain, and in September the patient reported for treatment. Roentgenographic examination at this time revealed an osteomyelitis of the right ramus (Fig. 1, above). Because the patient was comfortable and objected to being hospitalized, no treatment was instituted, but he was kept under observation. The patient continued on with his duties until February, 1944, at which time he was transferred to the hospital. It was at this time that he came under the care of the author.

Examination.—The physical examination was essentially negative except for the chronically draining fistula and slight tenderness to pressure over the right ramus. The intra-oral examination was negative. The tissue overlying the right mandibular third molar region appeared normal. The patient denied any injury to the face.

Roentgenographic Examination.—There was a radiolucent region approximately 2 cm. in diameter in the ramus just below the mandibular notch. There appeared to be a small sequestrum located within this region (Fig. 1, below).

Laboratory Findings.—The leukocyte count was 8,000. The blood sedimentation rate was 12 mm. A culture from the fistula revealed Staphyloccus albus. A urinalysis was negative for albumin and sugar. The reaction to the Kahn test for syphilis was negative.

Diagnosis.—Osteomyelitis of the right ramus (probably secondary hematogenous infection from the third molar region). In the author's opinion, the osteomyelitis was localized and the drainage resulted from sequestration, so preparation was made for sequestrectomy.

Surgical Procedure.—Penicillin was administered, beginning two days prior to the operation, as a prophylactic measure, 20,000 units every three hours. The patient was given premedication of morphine sulfate gr. ¼ and atropine sulfate gr. 1/150. After administration of thiopental sodium anesthesia, a vertical incision was made over the ramus. By using blunt dissection to prevent injury to the facial nerve, the external surface of the ramus was exposed sufficiently to allow adequate access to the field of operation. A complete debridement of the bony cavity was accomplished. A small sequestrum surrounded by granulation tissue was found within the cavity. The wound was loosely packed with iodoform gauze, allowing one end to protrude through the incision. The incision was closed with silk. A dressing was applied.

Postoperative Procedure.—Codeine sulfate gr. ½ with acetylsalicylic acid gr. 10 were given for sedation. An ice cap was applied to the jaw for twenty-four hours. The gauze pack was removed on the fifth day and replaced by another gauze dressing. Sutures were removed at this time. Penicillin was discontinued on the fifth day. The wound was dressed for a period of three weeks after which time it was healed fairly well. The patient was returned to a duty status with instructions to return for periodic examinations.

In May, 1944, the patient returned, stating that a week after his return to duty he had noticed

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Captain (DC), USN.
The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

a slight amount of drainage at the same location on his face. As the quantity was very small and he experienced no difficulty, he had neglected to return sooner. Roentgenographic examination (Fig. 2) disclosed a regeneration of bone with no apparent evidence of sequestration. Because of the small quantity of drainage and absence of other symptoms, it was decided not to interfere surgically at this particular time but to keep the patient under observation. For several months the patient was free of symptoms except for the previously mentioned exudate. During this period penicillin was given for ten days, 50,000 units every three hours. Roentgenotherapy and sulfathiazole, 1 Gm. every four hours, also were administered, all without beneficial results.

At the time of sequestrectomy great care had been taken to remove all material from the bony

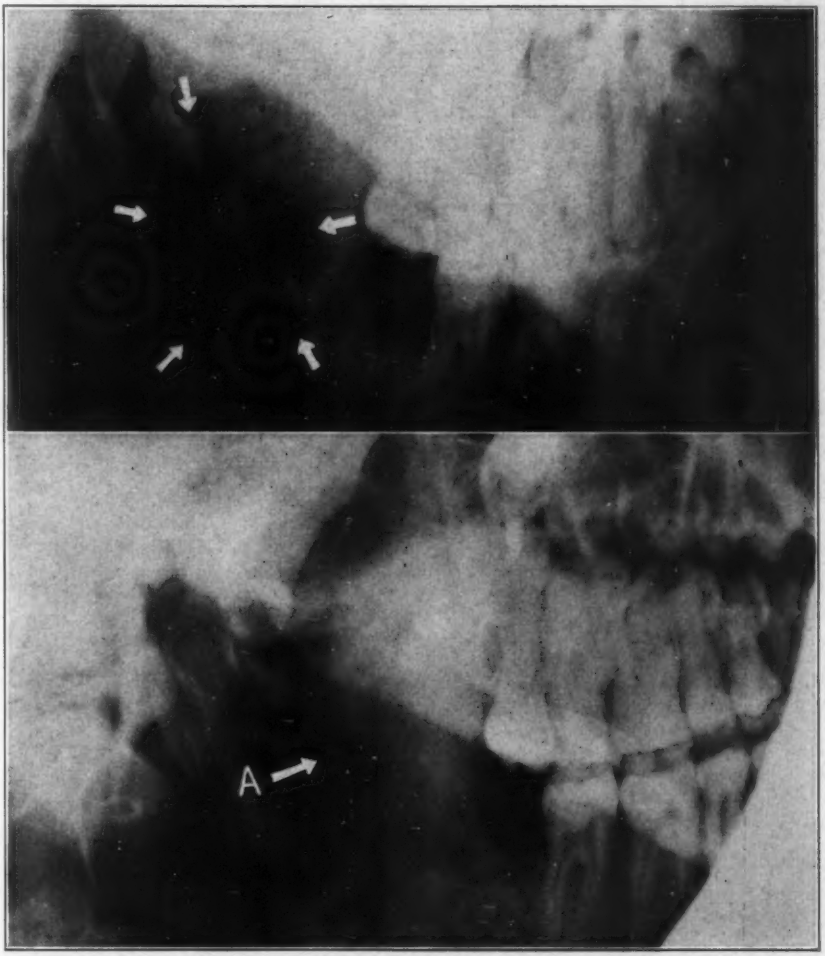

Fig. 1.—Roentgenograms of the ramus of the mandible. Above: Osteomyelitis (September, 1943). Below: Small sequestrum (A) (February, 1944)

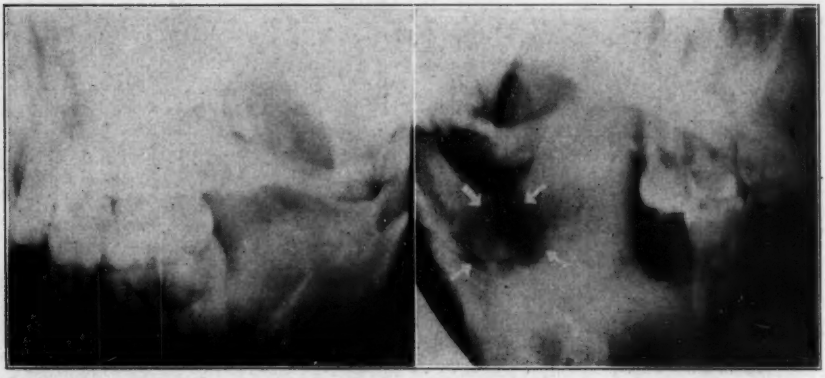

Fig. 2.—Roentgenogram taken in May, 1944, for comparison of normal left ramus and regenerating right ramus

cavity, and the surrounding bone had been normal in appearance. Therefore, it was considered inadvisable to submit the patient to surgery a second time without definite proof that the cause of drainage was at the site of the former field of operation. The decision was made to inject iodized poppy-seed oil (Lipiodol, Fougera) in the fistula for possible aid in establishing the source of the drainage.

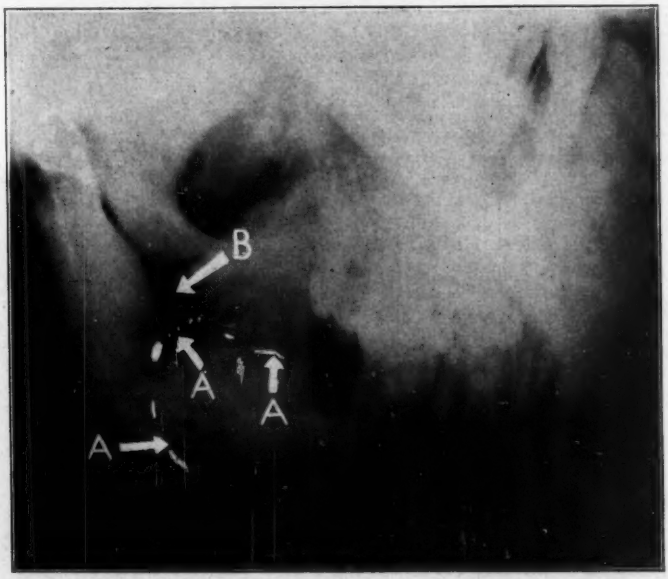

Fig. 3.—Lateral view of the ramus showing (A) Lipiodol in fistulous tracts (retouched) and (B) U-shaped loss of bone at the inferior border of the mandibular notch

Fig. 4.—Postero-anterior view showing the course of Lipiodol (A) in fistulous tracts (retouched)

Operative Procedure.—In September, 1944, Lipiodol was injected and roentgenographic examination of the ramus (lateral view, Fig. 3) showed excellent regeneration of the bone except for a U-shaped loss of bone at the inferior border of the mandibular notch. The Lipiodol could be traced to the bone and appeared to traverse the hole in the ramus to its internal surface. The postero-anterior view revealed the Lipiodol following a course down the internal surface of the ramus to the right mandibular third molar region (Fig. 4). The third molar region was negative in all roentgenographic examination.

Although the third molar region presented a normal picture, an exploratory operation of this region was indicated because of the previous history and the course of the Lipiodol.

Second Surgical Procedure.—In September, 1944, with the aid of conduction procaine anesthesia, a flap was elevated exposing the alveolar process in the third molar region. The soft tissue was dense and of a fibrous nature. The internal and external cortical plates of the alveolar process were extremely thick. The cancellous bone was necrotic with some pus present. Several small sequestrums and all necrotic bone were removed. The bony cavity was packed with iodoform gauze. Dressings were changed every few days and healing was uneventful.

Immediately after operative procedures there was no further drainage and the fistula disappeared. The patient soon afterward was transferred to a sea billet, but a note from him several months later stated that he had experienced no further difficulty.

Discussion.—One of the perplexing factors in this case was the absence of inflammation in the third molar region. Also the course of the fistulous tract was quite unusual. One explanation for the course of the fistula might be that, owing to the thickness of the cortical plates and dense fibrous overlying tissue, the line of least resistance was followed.—*United States Naval Air Station.*

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Biological Principles in the Treatment of Ununited Fractures. Dallas B. Phemister, in *Proc. Inst. Med. Chicago* 17:141 (June 15) 1948.

A better understanding of the biological properties of the callus in ununited fractures has resulted in the development of a more simple and efficient operative treatment than that generally employed. The usual causes of nonunion are local, the most important being (1) inadequate fixation which permits of continuous trauma to the callus, (2) displacement of fragments which interferes with the establishment of a fibrous bridge with impaction of coapted fragment ends from muscle pull which stimulates ossification, (3) infection of the fracture site, and (4) necrosis of the joint fragment in case of fractures bordering extensively on certain joints, as the hip. If one or a combination of these factors remains sufficiently active beyond the normal healing time, the callus fails to ossify or even to fill out the space between the fragment ends, and nonunion is established. It is widely assumed that in such cases the callus has become so altered that it can no longer be made to ossify, and that in order to obtain bony union it is necessary to break down the fracture, remove the intermediary and intramedullary callus, apply a bone graft and rigidly fix it to the fragments with metal screws.

It has been demonstrated that in case the fragments are in good position it is not necessary to break down the fracture, remove the callus, and fix the graft with screws. The fracture may be treated by the simple application of a strong bone graft to a leveled side of the fragments, suture of the overlying soft parts, and plaster immobilization for two to three months. Callus is thrown out from both the graft and the freshened surface of the shaft, and bony union is rapidly established between the two. The remaining old callus holds the fragments together and as motion is eliminated the intermediary callus, being less and less traumatized, becomes healthy and ossifies, and union of the fracture is usually present by the time the cast is removed. More than 100 such fractures have been treated in this simple way with reduction in time of operation and frequency of complications and with failure of union in but 4 cases. Only a relatively small number of ununited fractures of the shaft are so widely displaced that it is necessary to break down the fracture line, remove the intermediary callus, and align and rigidly fix the fragments to the bone graft with screws or wires.

A Case of Plasmocytoma of the Hard Palate. S. Sametnik, Tel-Aviv, Palestine. in *Acta Oto-laryng. orient.* 3:13 (Fasc. 1-2) 1947.

These are rather rare tumors which chiefly rise in the bone marrow and the lymphatic tissue of the nasopharynx. They are formed of true plasma cells or their immediate precursors.

An illustrative case is reported in a 37 year old Arab who had had a dull aching pain in the right cheek for about nine months and slight nose bleed several times during the past six months. The swollen cheek had existed two or three months. Examination showed a facial asymmetry caused by a large subcutaneous hematoma of the right cheek and infra-orbital area. There was a severe gingivitis with many bad or loose teeth and a soft swelling on the right side of the hard palate. Transillumination showed a dark right maxillary sinus with its basal opening blocked by blood clot. The histologic appearance of the swelling is described. These tumors chiefly rise from bone marrow or the lymphatic nasopharynx and are usually mistaken for malignant lymphosarcoma. They may develop a condition after months or years which is indistinguishable from multiple myelomatosis. The lesion is usually solitary so that radical excision or radiotherapy might prevent the fatal extension of the disease in the form of multiple myelomatosis. 8 references, 3 figures.—*Quart. Rev. Otorhinolaryng. & Bronch.-esoph.* Vol. 6, December, 1947.

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